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Charles Lester Hartsock, M.D.

Fellow, The Cleveland Clinic Foundation, 1921-1924
Staff Member, The Cleveland Clinic Foundation, 1924—
Division of Medicine, 1924—
Head, Department of Internal Medicine, and Senior Consultant

Born April 9, 1896
Died March 2, 1961

Charles Lester Hartsock, M.D.

ON March 2, 1961, the Cleveland Clinic lost the oldest active member of the Staff. Dr. Charles L. Hartsock passed away in the Cleveland Clinic Hospital after a month's illness from acute coronary thrombosis with ensuing cardiac decompensation. At the time of his death, Doctor Hartsock was Senior Consultant in Internal Medicine, having served previously as Head of the Department of Internal Medicine. His term of service at the Clinic spanned a period of forty years, longer than that of any other member of the Staff. He came to the Clinic as its first Fellow in July, 1921, a few months after its opening. Three years later, on July 1, 1924, he was appointed to the Staff.

Born on April 9, 1896, in Centerville, Pennsylvania, he lived during his early years at Cumberland, Maryland, where he received his primary education. Following undergraduate studies at St. John's College in Annapolis, Maryland, where he received his B.S. degree in 1916, he studied medicine at Johns Hopkins University in Baltimore, graduating there with an M.D. degree in 1920. He served an internship at Lakeside Hospital, Cleveland, in 1920 through 1921, before starting his Fellowship in Medicine at the Clinic on the service of Dr. John Phillips, one of the four Founders of the Clinic. Doctor Hartsock was certified by the American Board of Internal Medicine in 1937. His membership in many medical societies included the American College of Physicians, and the American Therapeutic Society — which he at one time served as vice-president.

Charlie Hartsock throughout his many years of practice was always the champion of sound clinical judgment; he emphasized particularly the importance of careful observation and interpretation of symptoms and signs. The welfare of the patient was always uppermost in his mind. He had a deep understanding of the psychology of those who are sick in mind and body. His special interests lay in the investigation and treatment of headache and diseases of the gastrointestinal system.

Doctor Hartsock had many interests aside from his profession. His avocation was floriculture, and he thoroughly enjoyed the cultivation of flowers both in his outdoor garden and his indoor orchid bed. During the period of architectural plan-

ning for the physical expansion of the Clinic building, he devoted much time and thought to the interior arrangements of the building, particularly the Department of Radiology. After his retirement, which was to have occurred this spring, his plan was to remain active in the management of the Shaker Savings Association, of which he was senior vice-president and a director.

He was firm in his opinions, a friendly and kindly man, and devoted to his family. He is survived by his wife, Doris; a son, John Phillips Hartsock; a daughter, Mrs. Paula Hartsock Thomas; and four grandchildren.

Those of us who were privileged to enjoy his friendship for so many years and to benefit by his wise counsel in dealing with difficult professional problems at the Clinic will always hold him in special esteem.

ALEXANDER T. BUNTS, M.D.

THE CLASSIFICATION AND DIAGNOSIS OF URINARY INCONTINENCE IN WOMEN

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WOMEN subject to urinary incontinence often are reluctant and ashamed to admit it, and they may be slow to seek medical attention because they believe that theirs is a unique disability. They curtail their social activities because of the constant insecurity resulting from unpredictable loss of urine with consequent odor and irritation. They may resort to various articles of protection, such as pads, rubber pants or aprons, and even towels, before seeking medical help. As a result, the physician who corrects the defect, and restores the patient's composure so that she may resume normal activities, will have an eternally grateful patient besides achieving great satisfaction himself.

The many causes of urinary incontinence make it imperative that a correct diagnostic evaluation be made if treatment is to be successful. A faulty diagnosis may lead to the wrong therapy that may make the condition considerably worse and thereby may jeopardize the results of secondary treatment. For these reasons, we propose to classify the types of urinary incontinence and to present the diagnostic studies we have found to be most helpful in evaluating this condition. The cooperative efforts of the gynecologist and the urologist are most desirable for thorough investigation of this complex problem.

Classification of Incontinence

There are five types of incontinence: (1) stress incontinence, (2) urgency incontinence, (3) dribbling incontinence with otherwise normal voiding, (4) dribbling incontinence with no voiding, (5) paradoxical or overflow incontinence.

(1) *Stress incontinence* is characterized by progressive involuntary loss of urine when physical activity such as coughing, sneezing, laughing, lifting, climbing stairs, or stooping, increases intraabdominal and intravesical pressure. This incontinence occurs with no preceding sensation of bladder distention or an urge to void. The extent of urinary loss may range from occasional dribbling associated with maximal stress, to extensive gushing occurring with only minimal exertion or positional change. Stress incontinence rarely occurs in nulliparous women, but typically occurs in parous women who have sustained occult lacerations during childbirth. There is loss of urethral support, and urethral resistance is unable to overcome increases in intravesical pressure. The onset of the condition is insidious

and it is progressive, becoming worse with menopausal atrophy.

Stress incontinence generally does not occur in the presence of a large cystocele, since increased intravesical pressure is transmitted away from the urethra rather than against the vesical neck. However, the surgical repair of a cystocele may produce stress incontinence by increasing the hydrostatic pressure on a lax urethra.

(2) *Urgency incontinence* is characterized by a feeling of fullness in the bladder, an uncontrollable urge to void, and subsequent precipitous loss of urine. Women with this type of incontinence have no urinary control when there is an urge to void. Urge incontinence may have a gradual or precipitous onset, and is not related to parity. It can be associated with stress incontinence, but it may occur independently. In the latter case, activity or stress will not result in urinary loss.

Several conditions will produce urge incontinence. Infections (including tuberculosis) may cause cystitis and urethritis that produce an irritable bladder; interstitial cystitis produces the same symptoms. Multiple sclerosis and cerebral vascular accidents may produce a neurogenic bladder characterized by uninhibited bladder contractions producing urge incontinence or "precipitous" micturition.

(3) *Dribbling incontinence with otherwise normal voiding* may be due to an ectopic ureter, a small vesicovaginal fistula, stress incontinence, a urethral diverticulum or an autonomous neurogenic bladder due to myelodysplasia or trauma to the sacral spinal cord.

An ectopic ureter emptying into the urethra or vagina produces symptoms that usually are first noted when complete continence cannot be achieved in childhood. In some women the loss of urine is so slight that the presenting complaint may be only a long-standing, persistent vaginal discharge. With a history of the onset of dribbling incontinence after a surgical procedure a search should be made for a small vesicovaginal or ureterovaginal fistula.

The early differentiation between a ureterovaginal fistula and a vesicovaginal fistula is important because a ureterovaginal fistula usually should be promptly corrected surgically in order to prevent stricture, hydronephrosis, and pyelonephritis. The surgical repair of a vesicovaginal fistula should be deferred until all local inflammatory changes have subsided. This generally requires three months, although a longer period may be desirable.

Constant dribbling with intermittent voiding may occur in women who have severe stress incontinence wherein urethral resistance is so low that any activity results in urinary loss.

A large urethral diverticulum often will fill with urine in the course of normal voiding. The diverticulum then will empty when the upright position is assumed. A chronically infected urethral diverticulum causes recurrent dysuria, irritative bladder symptoms, and dyspareunia.

The autonomous neurogenic bladder is often characterized by constant dribbling

with intermittent voiding. This occurs most frequently in children with myelomeningoceles or myelodysplasia, often associated with spina bifida. Trauma or tumors of the sacral spinal cord may occasionally produce this type of neurogenic bladder. The patient with an autonomous bladder voids in a characteristic manner by contracting the abdominal musculature and straining in the Valsalva manner. Pressure in the suprapubic area is also effective in emptying the bladder.

(4) *Dribbling incontinence with no voiding* usually occurs in association with a large vesicovaginal fistula that keeps the bladder constantly empty. The condition also exists in the presence of bilateral ureterovaginal fistulas or a unilateral ureterovaginal fistula when the opposite kidney is absent, or there is obstruction of the opposite ureter. A vesicovaginal fistula and a ureterovaginal fistula may coexist. Occasionally constant dribbling without voiding occurs when a neurogenic bladder is produced by lesions in the sacral cord as described above.

(5) *Paradoxical or overflow incontinence* is produced by an obstructive or neurologic lesion that prevents emptying of the bladder at voiding. The amount of residual urine insidiously increases, and the bladder distends until urethral resistance is exceeded and dribbling occurs. Often the patient has no discomfort associated with the distended bladder, and seeks medical aid because of the associated incontinence.

Diagnostic Evaluation

A careful history is of considerable assistance in evaluating the incontinent patient, since it often gives the clinician important clues in regard to the origin of the condition. It is helpful to know about previous surgical operations, and the time of onset and the degree of incontinence—on the basis of the amount of perineal protection that the patient requires. Many women have a minor degree of incontinence that is of little concern to them and thus may be of little concern to the physician. Incontinence may consist of constant dribbling, a loss of urine with stress, or may be secondary to an uncontrollable urge to void. Normal voiding may or may not occur. If there is normal voiding, the size and character of the urinary stream, the presence or absence of hesitancy, and of dysuria and hematuria are important considerations.

From the foregoing discussion, it is apparent that the patient's medical history is important, but only gives clues to the underlying cause of the incontinence, and aids in the selection of appropriate diagnostic tests and examinations. These procedures can be divided into two groups: (1) general examinations, used in all cases of incontinence; and (2) special examinations, used for specific conditions. The general examinations should include a general physical examination with special attention to the abdominal and pelvic examination, urinalysis, urography, and cystoscopy. The special examinations include the cystometric examination, cinefluorographic studies, special dye studies, and urethrography.

General Examinations

A pelvic examination is most helpful if it is performed in a systematic fashion. Abdominal palpation may reveal a large mass in the suprapubic area. Inspection of the external genitalia will demonstrate the presence or absence of local irritations and excoriations due to urinary loss. If the patient is asked to bear down or to cough, in the presence of stress incontinence or relaxations of the anterior vaginal wall, characteristic urethral rotation may be demonstrated and there may be a gush of urine through the urethral meatus. Urine may also issue from the vagina secondary to fistulous communications. Careful palpation of the anterior vaginal wall before instrumentation may reveal a thickening and tenderness of the urethra because of a urethral diverticulum. Frequently a diverticulum can be decompressed by digital pressure and its fluid can be seen to extrude through the urethral meatus. Fistulous defects may also be felt in the anterior vaginal wall.

The next step in careful pelvic examination involves inspection of the vagina. The Graves's speculum may be sufficient, although a Sims's speculum may be necessary to detect a small vesicovaginal or urethrovaginal fistula. The Sims's position may facilitate such an examination. The extent of pelvic floor relaxation can be determined by applying traction on the cervix with a tenaculum and urging the patient to bear down or to cough. Sometimes a cystocele can be detected only in the upright position.

Bimanual and rectovaginal examinations can be of great assistance, but should be reserved for the conclusion of the pelvic examination. In this manner, bladder sensitivity can be determined and a pelvic mass may be felt. When there is a cystic mass anterior to the cervix, catheterization should be employed to differentiate this mass from a distended bladder. Bimanual examination also will demonstrate a mass that impinges directly on the trigone of the bladder or pushes the cervix or uterus against the trigone. A previous suspension, ventral fixation or adhesion of the uterus to the anterior abdominal wall, secondary to cesarean section, can also be diagnosed.

Urinalysis is important, and a clean voided specimen may be examined initially, although a catheterized specimen is most desirable. If there is evidence of a urinary tract infection, culture and sensitivity studies should be obtained. In selected patients, specimens should be obtained to determine possible tuberculous involvement of the urinary tract.

Renal function studies are desirable as a routine procedure. A simple 15-minute phenolsulfonphthalein (P.S.P.) or urea clearance test will rapidly give an evaluation of the patient's renal status.

An *intravenous pyelogram* should be done on every patient with urinary incontinence. It provides a basis for estimating renal function and may demonstrate serious pathologic changes in the urinary tract which are asymptomatic. When incontinence occurs after a surgical procedure, or when the possibility of an ectopic

ureter exists, urography may provide definitive diagnostic evidence.

Panendoscopic and cystoscopic examinations are desirable preoperatively in all incontinent women. A fistula or diverticulum frequently can be diagnosed by the use of a panendoscope and a finger placed along the anterior vaginal wall. The panendoscope allows complete visualization of the urethra. Inspection of the bladder with the cystoscope will reveal whether or not pathologic changes are in the bladder which cause urge incontinence. A large, atonic bladder can be easily recognized and the presence of a vesicovaginal fistula frequently can be determined. Furthermore, the location of a fistula relative to the ureteral openings can be observed, and a catheter can be placed through a small fistula, for identification at the time of surgical repair. In the presence of tiny fistulas, local scarification or fulguration may encourage spontaneous healing. Ureteral catheterization with retrograde pyelograms may be helpful in determining the presence of a ureterovaginal fistula.

Special Examinations

The *cystometric examination* should not be overlooked as an aid in the evaluation of the incontinent patient. It can give valuable information that may indicate the desirability of medical treatment rather than an operative procedure.

The technic of cystometric examination is simple. The patient is instructed to void; then a Foley catheter is placed in the bladder and the amount of residual urine is measured. The Foley catheter is allowed to remain in situ while hot water and cold water are alternately run into the bladder. If the patient is unable to differentiate between hot and cold, the sensory side of bladder inervation has been interrupted. Then, water is allowed to run into the bladder in order to determine capacity and intravesical pressure (which is measured in centimeters of water) *(Fig. 1, A and B).* Uninhibited contractions can be noted, and in patients with extremely irritable bladders, methantheline bromide, U.S.P.,* given intravenously in a dose of from 75 to 100 mg. will differentiate between bladder spasm and uninhibited contractions. To determine the capacity of the bladder the patient is asked to indicate when filling reaches the point at which a maximal voiding urge is produced. The determination of the presence or absence of saddle anesthesia and the bulbocavernosus reflex completes the neurologic examination of the bladder. Before removing the Foley catheter, urethral length is measured and, with a special, calibrated catheter, urethral resistance is measured at one-half centimeter intervals along the urethra. The bladder is allowed to remain full, and after removal of the catheter, the extent of urinary continence can be determined in relation to quiet standing and stress.

When bladder dysfunction is of neurogenic origin, operative procedures tend to aggravate the problem, particularly if the patient already has a large amount of

*Banthine, G. D. Searle & Co.

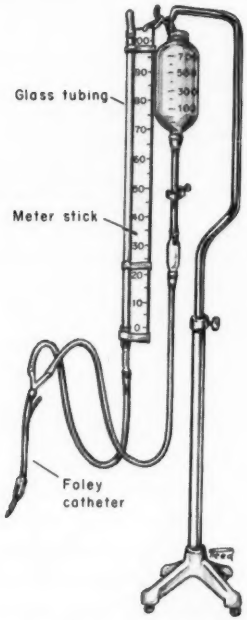
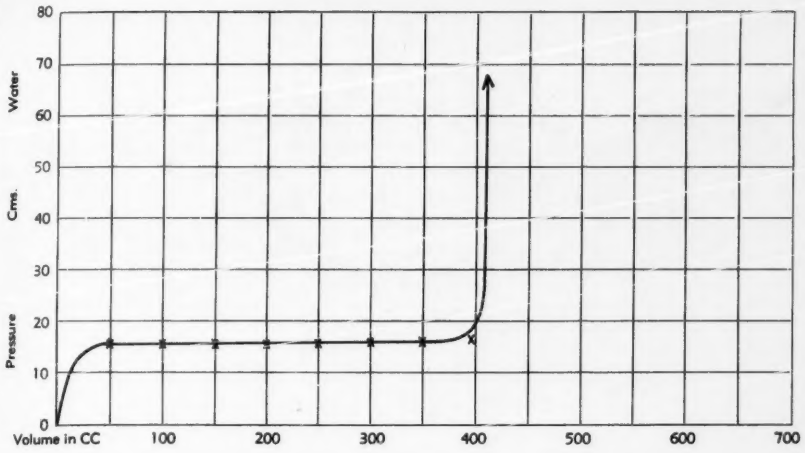


Fig. 1. A, Equipment for a cystometric examination.

residual urine. Banthine given orally, 50 mg. four times daily, often will produce great improvement by suppressing uninhibited contractions and thereby increasing the bladder capacity.

Cinefluorographic studies provide further assistance in the evaluation of stress incontinence. These studies employ cinefluorography of patients in the act of coughing, straining, and voiding. The technic consists of filling the bladder with a radiopaque contrast medium and using an image amplifier that makes it possible to take movies during these activities. The movies can then be reviewed for evidence of anatomic variations and defects. The technic is admittedly experimental, but we have found it to be of considerable assistance in providing evidence of the mechanisms involved in stress incontinence.

The differential diagnosis of fistulas may present a diagnostic problem, and the use of certain media will often be useful. When a small vesicovaginal fistula is present, a tampon may be placed in the vagina, and a dilute solution of methylene blue can be injected into the bladder through a catheter. After a few minutes the tampon is removed; if methylene blue is found on the tampon it indicates the presence of a fistulous tract *(Fig. 2A).* (In some patients it has been helpful to



Sensation to Heat Yes
—to Cold Yes
—to Distention Yes

First Desire 100

Uninhibited Contractions None

Voiding Average Amount
—Interrupted or Uninterrupted Stream
—Hesitancy None

Neurological Findings:
No saddle anesthesia
Intact bulbocavernosus reflex

Capacity —Supine 400
—Standing
Residual Urine 0

Clinical Diagnosis:
Normal bladder

Comment:

Fig. 1. B, Normal cystometrogram.

observe the apex of the vagina when introducing the methylene blue into the bladder.) When no fistulous tract is thus demonstrated, 1 ml. of indigo carmine should be given intravenously after a new tampon has been placed in the vagina *(Fig. 2B).* Indigo carmine is excreted by the kidneys, and if there is a ureterovaginal fistula, the dye will be found on the tampon. This dye may also help to identify ectopic ureteral orifices.

A urethrogram is of value in demonstrating urethral diverticula; *Figure 3* is a sketch showing the technic. An opening is made in a Foley catheter proximal to the bag, and the opening distal to the bag is closed. The Foley catheter is inserted into the bladder, the bag is inflated and is pulled tightly against the vesical neck. Contrast medium is inserted into the catheter and thereupon fills the urethra. If a diverticulum is present it often will become filled with the

Fig. 2. A, Sketch showing technic of demonstrating the presence of a ureterovaginal fistula by placing a tampon in the vagina and injecting indigo carmine intravenously. B, Sketch showing technic of demonstrating the presence of a vesicovaginal fistula by placing a tampon in the vagina and injecting methylene blue into the bladder via catheter.

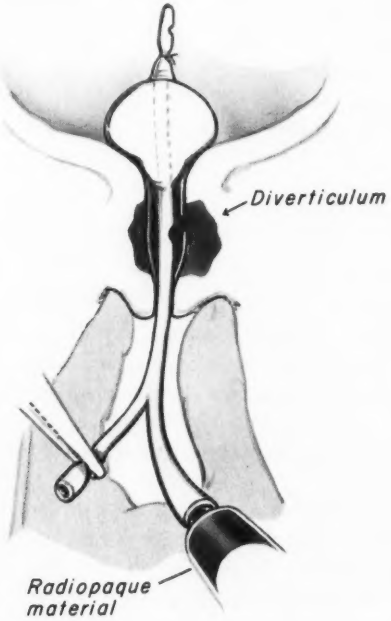


Fig. 3. Sketch showing technic of performing urethrography.

contrast medium and a urethrogram will demonstrate it. Special catheters are also available commercially for use in making urethrograms.

Conclusion

The classification of urinary incontinence and the diagnostic procedures we have found to be most helpful in determining the cause of incontinence, have been presented in detail. No attempt has been made to discuss therapy, but it is clear that it will be based on an exact determination of the cause of the incontinence. We advocate a thorough and critical evaluation of the incontinent woman, using the diagnostic procedures that we have presented.

DESICCATED THYROID AND *l*-TRIIODOTHYRONINE ADMINISTRATION IN HYPOMETABOLISM WITHOUT THYROIDAL DEFICIENCY

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NINETEEN patients having hypometabolism of nonthyroidal origin were studied to compare the therapeutic effects of desiccated thyroid and *l*-triiodothyronine. The ages of the patients ranged from 8 to 49 years. There were 6 females and 13 males.

Symptoms

The incidence of symptoms was as follows: obesity, 17 patients; fatigue, 10; drowsiness, 7; loss of hair and dry coarse hair, 3; suspicion of retarded sexual development, 3; mild mental depression, 2; headache, 2; hoarseness, 2; intolerance to cold, 1 patient; muscular and joint pain, 1; mild oligomenorrhea, 1; edema, 1. The relationship between the most common symptoms, obesity and fatigue, and the hypometabolism is not clear. They may appear as the most frequent symptoms in these patients only because they were the complaints that prompted the ordering of a metabolism test. The hypometabolism may have aggravated a tendency to obesity but apparently did not cause the fatigue.

The symptoms in these patients are of little value in ascertaining whether nonthyroidal hypometabolism or true hypothyroidism is present. Consequently, determinations of serum protein-bound iodine (PBI) concentrations, serum cholesterol concentrations, and thyroidal radioiodine† (I^{131})-uptake values were done.

Laboratory Findings Before Treatment

Basal metabolic rates ranged between −15 and −30. Sixteen of the 19 patients had basal metabolic rates of −20 or lower.

Serum cholesterol concentrations ranged from 104 to 257 mg. per 100 ml., the average being 178 mg. per 100 ml.

Serum PBI concentrations were determined in 16 of the patients. The values ranged between 4.0 and 9.0 μg. per 100 ml., the average being 5.8 μg. per 100 ml.

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†The radioactive material was obtained on authorization of the United States Atomic Energy Commission.

Thyroidal I^{131}-uptake was determined in 18 patients. Six-hour uptakes ranged from 13 to 26 per cent, the average being 18.9 per cent. Twenty-four hour uptakes ranged from 22 to 48 per cent, the average being 33 per cent.

Effect of thyroid-stimulating hormone (TSH) on thyroidal I^{131}-uptake. In each of five patients in whom the six-hour thyroidal I^{131}-uptake had been previously measured, 5 units of TSH was given subcutaneously. Fifteen hours after the injection of TSH, I^{131} was again administered and the six-hour thyroidal uptake was measured. Four of the five patients demonstrated an increase of 100 per cent or more in I^{131}-uptake after the administration of TSH. In the fifth patient the uptake was increased only from 14 to 18 per cent; this low I^{131}-uptake response may have resulted from the patient's inadvertently taking desiccated thyroid in a dose of 2 gr. daily up to the date of the test.

Treatment

Each patient received *l*-triiodothyronine* in divided doses totaling from 50 to 150 μg. daily, and desiccated thyroid,† from 2 to 6 gr. daily. The hormones were given in separate courses. Twenty-five micrograms of *l*-triiodothyronine was considered approximately equivalent in potential effect to 1 gr. of desiccated thyroid. Basal metabolic rates were determined in all patients at intervals of from one month to two months, and in some the thyroidal I^{131}-uptake, serum PBI, and serum cholesterol values also were determined. The symptoms of all patients were re-evaluated at intervals of approximately one month. The lengths of follow-up ranged from five months to three years.

Results

Table 1 records the basal metabolic rates in the 19 patients before and after treatment with desiccated thyroid and *l*-triiodothyronine, as well as a comparison of the effectiveness of the drugs.

Thirteen patients had no improvement in symptoms. In six patients there was slight improvement; in five of these, improvement was limited solely to a subjective sense of slightly increased energy. In the sixth patient, menses, mildly irregular before treatment, became normal after treatment.

In five of the six patients who experienced improvement in symptoms, the effects of the two drugs were equal. In the sixth patient, desiccated thyroid was more beneficial than *l*-triiodothyronine. In none was *l*-triiodothyronine more effective than desiccated thyroid.

In some patients the basal metabolic rate could be elevated by large doses of *l*-triiodothyronine (100 to 150 μg. daily) or desiccated thyroid (4 to 6 gr.

**Cytomel (liothyronine, synthetic l-triiodothyronine), furnished through the courtesy of Smith, Kline & French Laboratories.*

†Tablets of desiccated thyroid U.S.P., uncoated, Armour Laboratories.

daily). However, most of the basal metabolic rates remained at low pretreatment levels. In general, there was a striking absence of response of both the symptoms and the basal metabolic rates even to large doses of either hormone.

Table 1.—*Results of treatment of nonthyroidal hypometabolism with desiccated thyroid and l-triiodothyronine**

Patient	Dosage		Length of follow-up, months	Basal metabolic rate			Symptomatic improvement	Drug more effective
					After treatment			
	Desiccated thyroid, gr. daily	*l*-Triiodothyronine, μg. daily		Before treatment	Desiccated thyroid	*l*-Triiodothyronine		
1	4	100	9	−20	−11	−27	None	—
2	2	50	9	−21	−23	−24	Slight	Equal
3	2	50	6	−27	− 9	−16	None	—
4	3	150	12	−32	−26	−29	None	—
5	3	100	8	−23	−21	−24	None	—
6	6	150	26	−28	−11	−17	Slight	Equal
7	2	50	9	−27	−26	−26	None	—
8	3	50	12	−23	−18	−15	None	—
9	4	100	18	−22	−27	−24	None	—
10	4	100	24	−26	− 5	−11	Slight	Equal
11	6	75	32	−24	−18	−17	None	—
12	4	75	8	−25	−10	−24	None	—
13	3	75	6	−17	−16	−18	None	—
14	2	50	5	−21	+ 9	+ 2	Slight	Equal
15	3	75	7	−24	−16	−14	None	—
16	2	100	10	−29	−29	−25	None	—
17	6	150	8	−23	+ 5	−14	Slight	Thyroid
18	3	50	36	−15	− 8	−16	Slight	Equal
19	3	75	10	−19	−14	+ 8	None	—

*The hormones were given in separate courses.

Discussion

"Metabolic insufficiency,"[1] and "nonmyxedematous hypometabolism,"[2,3] are controversial terms that have been used by some authors in an attempt to denote a variety of symptoms (the most frequent being obesity and fatigue) and an abnormally low basal metabolic rate in the presence of normal results of other tests of thyroid function, including serum PBI, thyroidal I^{131}-uptake, and serum cholesterol determinations. It has been stated that *l*-triiodothyronine is more effective than desiccated thyroid in treating "metabolic insufficiency,"[1-5] but this

condition has been demonstrated not to depend upon a deficient production of thyroxin, and there are no data to support the contention that it results from a lack of *l*-triiodothyronine.

The biologic half-life of radiothyroxin was found by Lasker and Ryan[6] to be normal in three of four patients having "metabolic insufficiency"; and it has been suggested that the reason for the low basal metabolic rates is a disproportion between the mass of metabolizing cells and the mass of fat.[3] In another report[7] radiothyroxin was stated to be eliminated from the blood more slowly in patients having nonmyxedematous hypometabolism than in those having normal metabolism.

In four of our five patients to whom TSH was administered the response was active, indicating that the hypometabolism is not the result of primary thyroid failure. To our knowledge, TSH assays have not been reported as abnormal in this disorder.

The fact that our 19 patients tolerated relatively large doses of desiccated thyroid and *l*-triiodothyronine without overdosage manifestations suggests strongly that their symptoms were not the result of hypothyroidism. Thyroid-replacement therapy was peculiarly ineffective in these 19 patients. When there are an adequate concentration of thyroid hormone in the blood and a lack of cellular response, clinical myxedema should be present; but in these patients it is not. Further study is required to determine whether a basal metabolic rate that is only mildly or moderately depressed is truly abnormal for the individual involved, and, if it is abnormal, to ascertain its cause.

We agree with Keating[8] that to consider "metabolic insufficiency" as a disease entity or as a syndrome is erroneous. The well-controlled studies of Levin,[9] Sikkema,[10] and Goldberg[11] support such a view.

Summary

A group of 19 patients who had symptoms suggestive of hypothyroidism and low basal metabolic rates, but in whom other tests of thyroidal function were normal, did not respond significantly to the administration of *l*-triiodothyronine or equivalent doses of desiccated thyroid.

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HEAT AS AN ADJUNCT TO THE TREATMENT OF CANCER

Experimental Studies

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MANY cancers are more susceptible to destruction by heat than are the tissues they grow in. Heat acts synergistically, or at least additively, with radiation so that the combined effects of the two are greater than the effect of either one alone. These observations were reported half a century ago,[1,2] but for the past 20 years little has been published on the effects of heat on cancer.

Our interest in the effects of heat started in June, 1960, when, unaware of previously published studies, we noticed the regression of a mouse tumor that had been exposed to a temperature of 42 C. (107.6 F.) for two hours. The effect was reproducible. When we implanted S91 melanomas on the feet of DBA_1 mice we were able to destroy some of the resulting tumors by immersing the tumor-bearing feet for 30 minutes in water at 44 C. This temperature is only 111.2 F. or the temperature of a comfortably hot bath. In most cases there was no damage to the normal tissues of the feet. All of the animals that appeared to be cured 21 days after treatment lived longer than 90 days without recurrence.

The S91 melanoma is a moderately radioresistant tumor whose progressive growth is not controlled by radiation in doses up to 1000 r. But when this tumor was heated for 30 minutes at 44 C. and immediately treated with 1000 r there was complete regression in 20 of 25 mice. Twenty control mice, whose tumor-bearing feet were immersed in water at 37 C., showed progressive growth of their tumors, and 75 per cent of the animals were dead in 31 days. It appeared that heat selectively killed many tumors without damaging surrounding tissues, and that it acted synergistically with radiation.

Materials and Methods

The literature for the past 15 years was searched for information on the effects of heat on tumor growth without finding any major studies on this subject. Further studies then were made on the effects of heat on tumors, but since there was difficulty in obtaining an adequate supply of DBA_1 mice, we used female Swiss mice three to four weeks old, and a transplantable tumor, sarcoma 180* (S180) that grows rapidly but does not metastasize.

The author expresses his appreciation to Dr. F. W. O'Brien, Jr., and to Dr. D. G. Smith (Fellow), of the Division of Radiology, for their help in the radiologic aspects of this study, and to Mrs. V. Mirkovitch for her help and suggestions in the technical aspects of the heating.

**Obtained from Arthur D. Little & Associates, Boston, Massachusetts.*

The tumor strain was maintained by injection into the flanks of the mice. The resulting tumors were excised, minced, suspended in an equal amount of Hank's solution, and the tumor fragments were injected with a 20-gauge needle into the web of a hind foot. Tumors usually appeared within three days, and within eight days were about 1 cm. in diameter. Spontaneous regressions never occurred within the first three weeks, but thereafter did occur in 9 per cent of 120 mice, usually associated with ulceration of the tumor or with its being eaten by the mouse.

A week after implantation, when the tumors were about 1 cm. in diameter, the tumor-bearing feet were immersed in a water bath at the desired temperature. To hold the tumor in the bath, the mouse was restrained with adhesive tape in stocks made of a piece of sheet lead, 5 cm. by 13 cm. by 0.1 cm., with a slot 5 cm. long and 0.3 cm. wide through which the tumor-bearing foot was passed. A rubber washer, 1 cm. thick and slit on one side so that it could be opened, was applied on the leg above the tumor to hold the tumor down into the water *(Fig. 1)*. The mice were then placed on a test tube rack, with their tumor-bearing feet

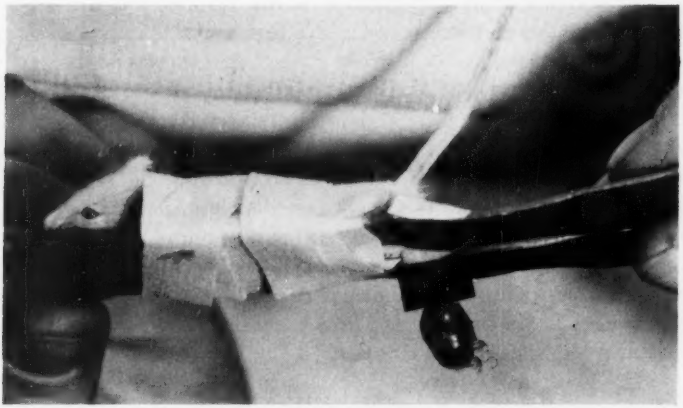

Fig. 1. Mouse restrained on sheet lead with tumor-bearing foot protruding through slot in the lead.

in the water *(Fig. 2)*. Radiation, given by a 200-kv. machine, was applied with the mouse's foot toward the radiation source and the lead shielding the body. Using this system, the following observations were made.

Observations on the Effects of Heat on Transplantable Tumors in Mice

(1) *Between 42 C. and 47 C. the time of exposure required to destroy S180 implanted on mice's feet can be halved for each degree of Centigrade that the temperature is elevated.*

The destructive effect of heat on tumors began at about 41 C., but at this temperature many hours of constant exposure were required. At 42 C., 120 minutes

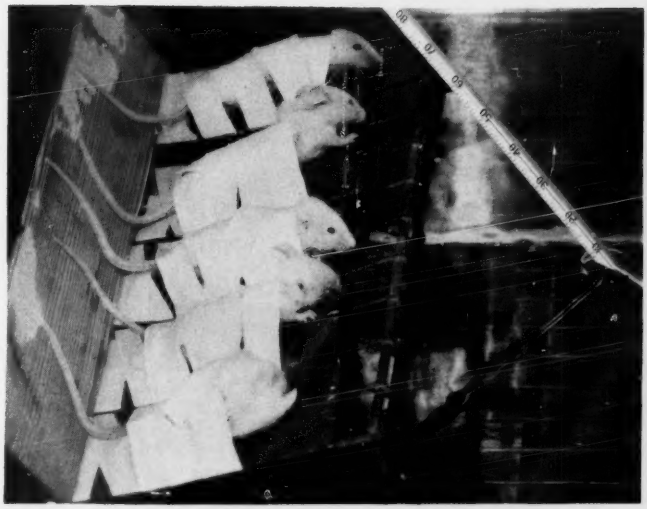

Fig. 2. Method of heating the tumor-bearing feet in a water bath.

was required to destroy S180 in more than 50 per cent of the mice treated; at 43 C., 60 minutes; at 44 C., 30 minutes; at 45 C., 15 minutes; and at 46 C., only seven and one-half minutes. In these tests the tumors were destroyed in 49 of 67 mice. Thus, from 42 C. through 46 C., a similar biologic effect was obtained by doubling the time exposure for each degree that the temperature was reduced. In this range of temperature, the time required to destroy the tumor can be expressed by an exponential curve *(Fig. 3)*. A similar exponential curve *(Fig. 4)*, with longer exposures at each temperature, expresses the exposure to heat that damaged the normal feet of DBA_1 mice to such an extent that the treated feet of half of the mice dropped off within a week of treatment.

Above 46 C., the heat capacity of the skin, and the lag of the tissues in transmitting the heat of the water bath to the center of the tumor, distort the exponential curve. According to the formula that expresses the effects of heat in the range of 42 C. through 46 C., an exposure of less than one minute at 49 C. should suffice to destroy the tumor. But in one minute's exposure of the tumor-bearing foot in a bath at 49 C., there is not time for the heat at the center of the tumor, measured by thermocouple, to reach a temperature higher than 46 C. An exposure of one minute at this temperature does not destroy the tumor. If the time of treatment is prolonged to four or five minutes so that the cells at the center of the tumor are given enough exposure to be destroyed, the exposure of the skin will exceed its threshold of tolerance and it will be scalded. Therefore, exposures at high temperatures in water baths do not effect cures without damaging normal

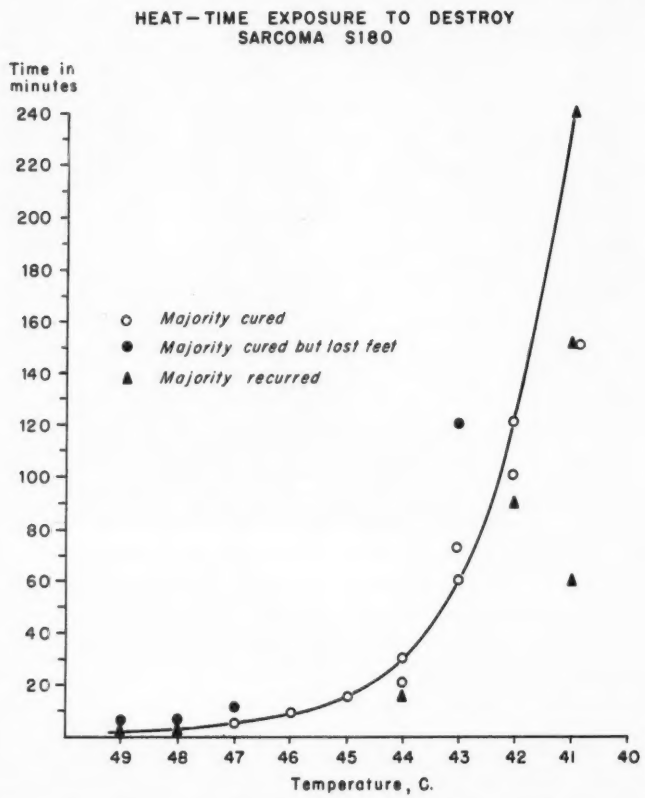

Fig. 3. Exponential curve expressing duration of exposure, in minutes, which is required at various temperatures to destroy the majority of S180 tumors implanted on the feet of Swiss mice. Each dot represents an experiment of from five to eight mice.

tissues; whereas, longer treatments at temperatures in the range of 46 C. through 42 C. are effective. Forty-four degrees Centigrade for 30 minutes proved to be the most convenient and effective exposure to destroy the majority of S180 tumors implanted on the feet of Swiss mice.

(2) *The destructive effects of heat are visible immediately after exposure of the tumor.* There is cyanosis of the tumor-bearing part of the foot; the cut surface of the tumor is dark red; and microscopically there is striking dilatation of blood vessels and hemorrhage into the tumor. If the tumor is large in proportion to the size of the mouse (i.e., more than 2 cm. in diameter in a four-week-old Swiss mouse) the mouse dies within from 10 minutes to 24 hours after treatment, perhaps as a result of shock from loss of blood or fluid into the tumor, or perhaps as a result

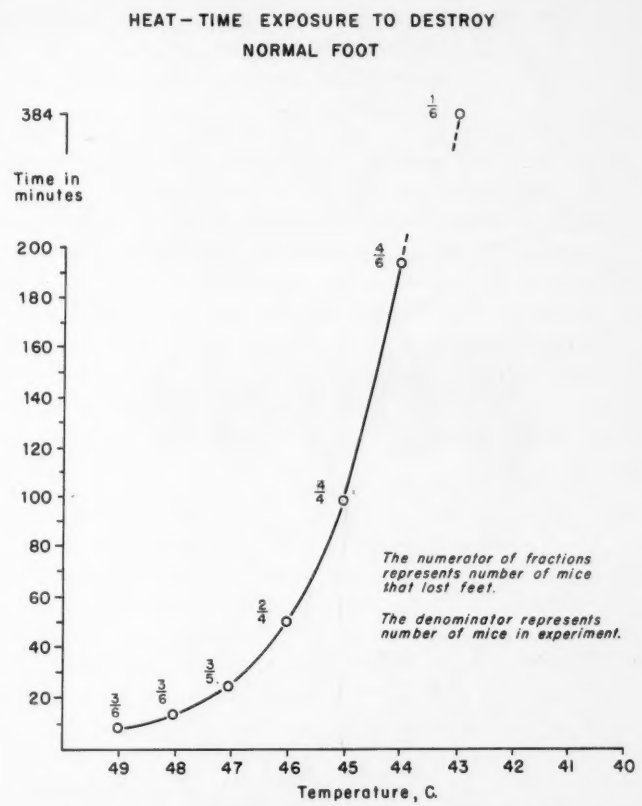

Fig. 4. Exponential curve expressing duration of exposure, in minutes, which is required at various temperatures to destroy the majority of heated feet in DBA_1 mice.

of toxic metabolites from the treated area.

(3) *When the exposure to heat has been in the therapeutic range, the tumor turns black within 24 hours after treatment, and in the next few days becomes a dry scab that falls off about the seventh day, leaving the remainder of the foot intact.* Sometimes the death of the tumor is less abrupt, and it seems to be resorbed and to disappear without death of the overlying skin. When the tumor is more than 1 cm. in diameter and dies suddenly, the mouse may lose its foot in the course of the rapid necrosis of the tumor. Sometimes a mouse chews off its own foot. Usually the tumor sloughs off and leaves the foot scarred but intact *(Fig. 5)*.

(4) *If recurrence takes place, it appears promptly, usually within two weeks.* Late recurrences were not observed in 28 mice that appeared to be cured three weeks

after treatment and were followed for 40 or more days. Ten "cured" mice have been observed for longer than nine months without evidence of recurrence. In this respect the effects of heat differ from those of radiation, in which late recurrences after primary regressions are common.

(5) *At temperatures between 42 C. and 46 C. the time of exposure required to destroy the majority of normal feet is more than twice the time necessary to destroy the majority of S180 tumors implanted on feet.* This relationship provides a relatively broad range of therapeutic exposure in which the tumor is destroyed without irreversible damage to normal tissue. Above this range there is a high incidence of damage to normal tissues.

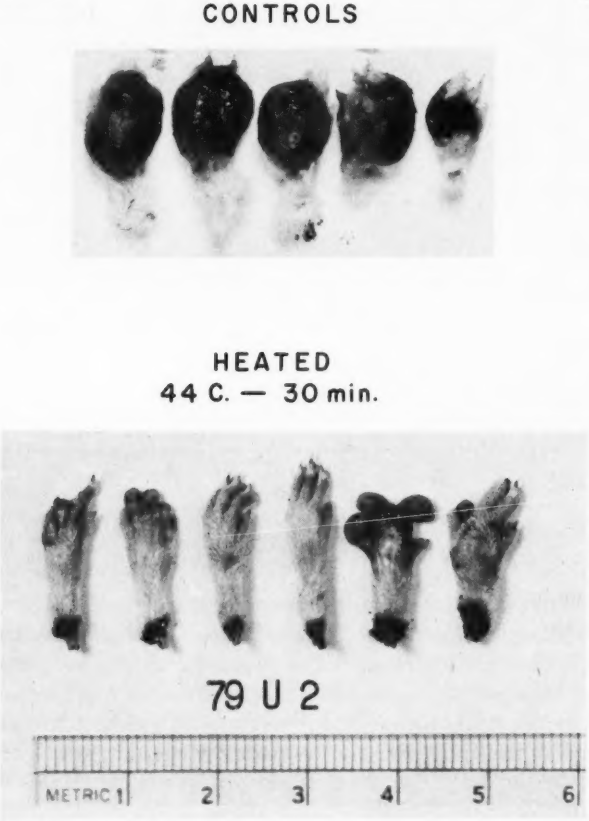

Fig. 5. Feet of mice on which S180 had been implanted. Control mice received no treatment and were photographed soon after the other mice had been treated. Treated mice were exposed to 44 C. for 30 minutes and were photographed one month after treatment.

(6) *Exposure of a tumor to heat for a period of time shorter than that required to destroy it, makes the tumor temporarily resistant to subsequently applied heat.* In each of 12 mice a single exposure of the tumor to 44 C. for 10 minutes, made the tumor so resistant to subsequent treatment that the next day it was undamaged by exposure of 30 minutes at 44 C., a dose that destroyed more than 70 per cent of previously unheated tumors. This acquired resistance to heat appears to be the result of a biologic adaptation of the cells and is associated with the disappearance of all mitotic figures. It could be likened to the transformation of heat-sensitive bacteria into heat-resistant spores. Fractionated treatment, consisting of exposure to 44 C. for 10 minutes daily for five days, slows the growth of a tumor but does not destroy it. The same is true of heating at 42 C. for 90 minutes followed in four days by repetition of the same treatment. In this respect the effects of heat appear to differ from those of radiation. There does not seem to be a cumulative effect of small treatments that ultimately destroys the tumor.

(7) *Conventional anticancer drugs do not seem to enhance the destructive effects of heat on tumors.* For example, 5-fluorouracil, in doses of 25 mg. per kilogram of body weight, injected daily for two days before heat treatment and for three days after, had no additive or synergistic effect. In 26 mice treated at various exposures to heat alone there were 14 recurrences. In 24 mice treated by 5-fluorouracil and identical exposures to heat there were also 14 recurrences. In small pilot experiments Thio-Tepa* injected intraperitoneally during the heat treatment in a dose of 10 mg. per gram of body weight did not alter the incidence of regression, nor did 75 micrograms per kilogram of body weight of actinomycin D, injected for five days before heating S91 melanomas.

Distilled water injected into the tumors before they were heated did not change the effect of heat. This experiment, however, was unsatisfactory because the water often escaped through the needle tract.

Application of a tight rubber band above the tumor during the heat treatment resulted in more frequent loss of the foot, but had no significant effect on the tumor's response to heat. At room temperature, application of a tourniquet above the tumor for half an hour did not cause either necrosis or regression of the tumor.

Because alcohol is an enzymatic poison that causes coagulation of protein at low temperatures we studied its effects on heated tumors. Fifty per cent alcohol, injected into the stomach, in doses of 0.3 ml. was sufficient to make a mouse stagger and lose coordination. When the tumors of 10 intoxicated mice were heated for 20 minutes at 44 C., the tumors were destroyed in three of them; whereas in none of 20 mice that were not given alcohol were the tumors controlled at this exposure. In the mice treated with heat and alcohol the growth of the tumors was retarded significantly as compared with that of the mice treated by heat alone. It is possible that alcohol affects the same enzymatic system that causes tissues to be more suscep-

*Thio-Tepa (N^1, N^1, N^{11}, *triethylenethiophosphoramide*), Lederle Laboratories.

tible to destruction by radiation at high oxygen tensions. The field of synergism of chemicals with heat requires further investigation.

(8) *Heat enhances the effect of radiation on tumors, and radiation enhances the effect of heat.* Treatment of S180 for 15 minutes at 44 C. (instead of for the 30 minutes that is required to kill the tumor) did not increase the incidence of regressions above that occurring in untreated control mice. In another experiment, exposures to 1000 r caused regression in 25 per cent of the mice compared to 9 per cent in untreated control animals. Combining heat at 44 C. for 15 minutes with 1000 r given immediately, raised the rate of cure to 75 per cent, and it made no difference whether the tumors were heated first or radiated first. Results of a typical experiment are shown in *Table 1.*

Table 1.—*Results of treatment of sarcoma 180 on feet of Swiss mice followed 75 days*

Type of treatment	Total number of mice	Number of mice		
		Tumor controlled	Lost foot	Died of recurrence
None	8	1 (Late spontaneous regression)	0	7
Heat alone				
44 C. for 15 min.	8	0	0	8
44 C. for 30 min.	19	13	4	2
Radiation alone				
500 r	4	1 (Late spontaneous regression)	0	3
1000 r	16	5	1	10
1500 r	4	0	1	3
Heat and radiation				
44 C. for 15 min. + 500 r	12	5	0	7
44 C. for 15 min. + 1000 r	12	8	1	3

Another type of tumor, the S91 melanoma, in DBA_1 mice is more resistant either to heat or to radiation than is S180, yet as mentioned in section 1 this type of tumor also was controlled by combining heat and radiation *(Fig. 6).* It was difficult to cure the melanoma by either heat alone or radiation alone without using exposures that caused irreversible damage to normal tissues. The reason for the effectiveness of combined therapy in controlling the tumor without damage to the feet may be that the peak of the reaction to heat and the peak of the reac-

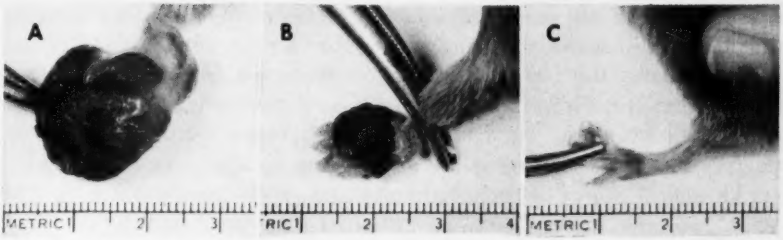

Fig. 6. A = heat alone; B = radiation alone; C = heat and radiation (same doses as in A and B). Synergistic effect of heat and radiation shown by complete control of S91 melanoma in DBA_1 mouse. Neither treatment given alone controlled the tumor.

tion to radiation occur at different times, the heat effect being immediate and the radiation effect being delayed; or it may be that a synergistic effect is exerted selectively on the tumor as compared with the normal tissues.

(9) *It is unlikely that immunologic mechanisms are responsible for the disappearance of heated tumors.* The effect is too prompt for an immunologic reaction and, furthermore, after a tumor on one foot has been controlled by heat, challenge of the contralateral foot by injection of new tumor cells usually is followed by growth of tumor. Twenty-six mice whose tumors had been destroyed by heat, from one to two months earlier, were challenged by reinjection of the same tumor strain on the opposite feet. In 22 the tumor grew progressively and killed 20 of the mice within 33 days.

(10) *Tumor cells in vitro withstand more heat than they do in vivo.* Minced tumor cells suspended in Hank's solution and heated in a sealed tuberculin syringe at 45 C. for 15 minutes (an exposure that would destroy S180 in vivo) were still viable and produced tumors in all of 11 mice. However, the first appearance of the tumors was retarded and in the beginning they grew more slowly than usual. In another experiment, when minced tumor was heated to 49 C. for six minutes and was injected into 9 mice, the tumors did not appear for 14 days, compared with three days for tumors arising from unheated cells. Twenty-one days after the heated cells were injected all the mice had tumors.

In one pilot experiment involving 36 mice, tumors from heated cells that had been separated from one another, by passage through a cytosieve, appeared five days earlier than those from tumors that were merely minced. The opposite was true when the cells were not heated, the tumors arising from minced tumor appearing four days earlier than those arising from tumor cells passed through a cytosieve.

These results suggest that heated tumors or their hosts make some substance that is toxic to the tumor and destroys it. Experiments on 24 mice whose tumors were heated in vivo support this hypothesis. When the tumor-bearing feet were exposed to 44 C. for 40 minutes, and tumor cells were transplanted immediately

after heating, the cells grew as well as those of unheated tumors. But when the tumor was left intact on the living mouse for four hours after heating, and then was transplanted, the time of appearance of tumors was delayed for two or three weeks beyond the time of appearance of those that were transplanted immediately, and in two of the twelve mice no tumors appeared.

(11) *The growth of tumors may be temporarily slowed by heat even when the tumors are not killed.* Tumors that are heated sublethally at first shrink and then for a few days grow more slowly than usual. Mitotic figures disappear from the tumor, and often there are cellular changes that pathologists describe as similar to those seen after radiation. Later the tumor may resume its usual rate of growth or may grow more rapidly than unheated tumors.

(12) *There are differences between normal and malignant tissues in their tolerances to heat, and there are also differences between various types of tumor and between various types of normal tissue.*

S180, which grows rapidly, is extremely sensitive to destruction by heat; the S91 melanoma, which grows slowly, is moderately sensitive to heat; and the carcinosarcoma in C57, which grows almost as rapidly as the S180 and much more rapidly than the melanoma, is so resistant that we have not yet been able to control it permanently either by heat alone or by radiation alone without damage to the foot.

Not only tumors, but tissues vary in their sensitivity to heat. The tail of the mouse is more easily destroyed by heat than is the foot. Results of pilot experiments designed to test the tolerance of mucous membranes of the mouth and rectum suggest that they may be more tolerant of heat than is the skin. Perhaps the higher the normal temperature of the tissue the higher is its tolerance to heat.

The Use of Heat in the Treatment of Cancer by Other Investigators

At this point in our studies, we came upon the work of Warren[3] who in 1935 reported on induced systemic hyperthermia as an adjunct to roentgentherapy in the treatment of patients with advanced cancers. We then reviewed the literature of the 1920s and 1930s and found a number of excellent studies on the biologic effects of heat and radiation, among which were Rohdenburg and Prime's[4] classic paper, published in 1921, and Westermark's[5] work with rat tumors in 1927. Our studies had confirmed the results of these earlier investigations. Similar results have been reported by Selawry, Goldstein, and McCormick[6] working with cancer cells in tissue culture. Since Selawry, Carlson, and Moore's[7] review summarizes observations made on the biologic effects of heat and radiation up to 1958, and since Westermark[4] reports in detail the many successful applications of heat to the treatment of human tumors, I shall not cite the old literature in detail. It can be summarized by saying that 50 years ago exposure to temperatures between 41 C. and 49 C. was extensively and apparently successfully used in the treatment

of cancer both in man and in laboratory animals. From the reports that have been published and from our own observations the following conclusions can be drawn:

(1) The destructive effect of heat does not depend on temperature alone, but on the duration of exposure at a critical temperature.

Some cancers in animals and in man are more susceptible to destruction by prolonged exposures to temperatures between 41 C. and 50 C. than are the normal tissues around them.

(2) Heat and radiation act synergistically, or at least additively, to effect destruction both of normal and of malignant tissues.

Effect of Heat on Spontaneous Tumors in Animals

The effects of heat on spontaneous tumors in several animals besides mice were studied. Three illustrative case reports are presented.

Case 1. A pet female rabbit several years old was brought to us with a tumor of the ear, 1.5 cm. in diameter and 1.5 cm. thick. A biopsy specimen showed an anaplastic histiocytic tumor with many inclusion bodies. The ear was immersed in a water bath at 47 C. for 15 minutes. Three days later the tumor fell off. A week after treatment, a biopsy specimen of the remaining ulcer showed no tumor. There was no damage to the ear, and healing was complete within two weeks. Four months after treatment, there was no recurrence. Pathologists believe that this was a tumor of viral origin.

Case 2. A 17-year-old female mongrel dog was brought to us by F. A. Coy, D.V.M., with an osteogenic carcinoma, the size of a golf ball on the tip of the lower jaw. During the previous year it had recurred five times after curettage and exposure to 1400 r. The diagnosis was confirmed histologically.

Under intratracheal anesthesia the dog's mouth was held open with a gag and the tumor-bearing jaw was immersed in water at from 48 to 49 C. for one hour. During treatment, the temperature of the center of the tumor, measured by thermocouple, was 44 to 46 C. After the treatment the tumor was cyanotic, and three days later sloughed off, leaving the jaw intact. A week after treatment a biopsy specimen of the jaw showed no tumor. The dog incurred no damage except a second-degree burn of the chin, which re-epithelized rapidly. The mucous membrane of the mouth was not damaged.

One month after treatment, a biopsy specimen of the jaw showed recurrence, and the dog was given a second hot-water bath treatment of one hour at 49 C. Again there was sloughing, and a week later a biopsy specimen of the cleanly granulating jaw showed no tumor. Eight weeks after the last treatment, there was a second recurrence that was treated by a combination of heat by microwave diathermy and 1000 r of cobalt-60* teletherapy. This resulted in necrosis of the tumor and slough of the tip of the jaw. The dog died two weeks after the last treatment with quadriplegia of unknown origin. Microscopic examination showed viable tumor still present at the periphery of the treated field.

**The radioactive material was obtained on authorization of the United States Atomic Energy Commission.*

Case 3. A female boxer dog had a proved mast-cell tumor of the ankle that had recurred three times in a year after local excisions and was the size of a golf ball *(Fig. 7A)*. Mast-cell tumors in the dog are similar in their clinical behavior to reticulum-cell sarcomas in man. The dog also had a huge tumor of the shoulder.

The pad of the dog's foot was protected with a plastic boot, and to facilitate conduction of heat, the tumor-bearing part of the foreleg was shaved. The leg up to mid-thigh then was immersed in water at 49 C. for one hour, digital pressure being maintained on the femoral artery most of the time to diminish the cooling effect of blood flow. The temperature of the center of the tumor, measured by thermocouple, ranged between 42 C. and 45 C.

After treatment, the skin over the tumor was slightly cyanotic. Two days later the tumor was softer and smaller than before treament. By the fourth day, the tumor had disappeared and the underlying bone was easily palpable. Ten days after treatment the tumor had vanished, leaving a small concavity. There was superficial damage to the outer layer of the shaved skin over the tumor and breakdown of the thin epithelium of the former surgical scars. All areas healed promptly *(Fig. 7B)*. Six weeks after treatment the tumor recurred and was treated again, this time by a combination of heat and radiation; and again it disappeared. The dog died three weeks after treatment, as a result of its other tumor. Sections of the ankle showed no viable tumor.

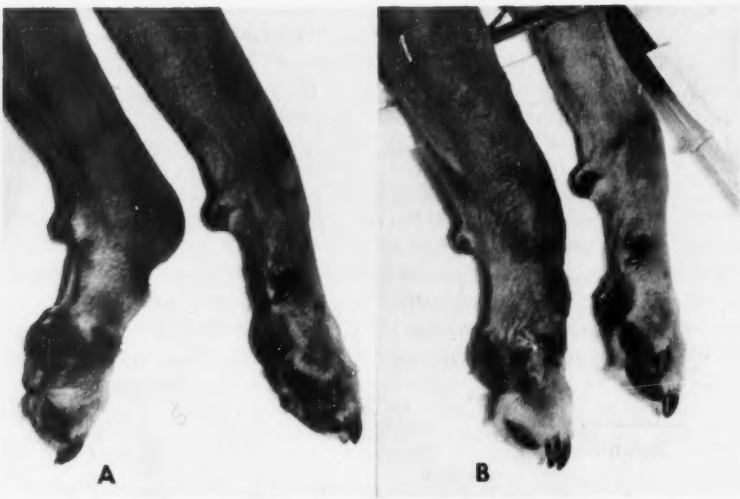

Fig. 7. A, Mast-cell tumor of dog's ankle before treatment. B, Dog's ankle one week after immersion in water bath at 49 C. for one hour.

Tests of Heat Sensitivity of Human Cancer

Metastatic cancer of the breast. In three patients with extensive intracutaneous

metastasis of breast cancer, proved by biopsy, a small area of the involved skin was treated by moist hot packs or hot water, the exposures ranging from 24 hours at 42 C. to one-half hour at 48 C. In each case there was striking regression of cancer in the heated area. The induration and nodularity of the skin vanished within seven days. In the patient treated at 42 C. for 24 hours there was a small superficial second-degree burn in the heated area.

In each of the three patients, in spite of disappearances of gross tumor, microscopic cancer was still evident in biopsy specimens.

Metastatic cancer of the stomach. Intracutaneous metastases of a cancer of the stomach were heated in the same way as the breast cancers but showed no regression of the skin nodules following exposure sufficient to cause a small superficial blister.

Recurrent cancer of the colon. The heat sensitivity of a fungating pelvic radioresistant recurrence of a sigmoid cancer was studied by observing the reaction of the tumor to irrigation with hot water. Under anesthesia, 250 gm. of necrotic tumor that filled the rectum, vagina, and ischiorectal space was scooped out and a mushroom catheter was inserted in the cavity. The cavity was then irrigated with water at 50 C. for 20 minutes, during which time the vagina and skin were cooled by a spray of cold water. Radiation of 1000 r was administered by cobalt-60 teletherapy immediately after the heat. Two weeks after the treatment there was no damage to the normal tissues and there were no visible fungations. Cancer was still present microscopically deep in the fibrous tissue but the fungating part of the tumor had been destroyed. A month later it recurred.

Cancer of the rectum. The heat sensitivity of a large, low-lying rectal carcinoma has been tested. It was a typical adenocarcinoma grade 3 with raised edges and a central crater involving two thirds of the circumference of the bowel. Its location indicated treatment by abdominoperineal resection. In view of the reported advantages of preoperative radiation in the treatment of rectal cancers, it was decided to treat the tumor preoperatively by a combination of radiation and heat.

The heat was applied by water at 50 C. With the patient under caudal anesthesia in the Kraske position a large Bakelite proctoscope was inserted in the rectum and through this a Foley catheter was passed beyond the tumor into the colon. The bag was then inflated and the catheter was pulled down until the bag rested snugly against the tumor, thus isolating the tumor and the rectum from the rest of the colon. The isolated tumor-bearing segment of the rectum then was filled with water at 50 C. and was replenished with hot water so that the temperature was kept constantly between 50 C. and 51 C. for 15 minutes. Biopsies were performed immediately before and immediately after the treatment; there was no histologic change as the result of the heat treatment. Immediately after the heat treament, 1000 r of cobalt-60 teletherapy was administered.

The next day there was tenderness of the anus and a profuse dark-brown dis-

charge. On the second day after treatment, the lower part of the tumor was inspected through a proctoscope, and showed sloughing necrotic tumor, but no trace of viable tumor for biopsy. A week after the heat and radiation treatment, abdominoperineal resection was done. There was no evidence of metastasis and nothing unusual about the external appearance of the bowel.

When the removed rectum was opened, the rolled edge of the upper part of the tumor against which the Foley bag had rested looked the same as the rolled edge of any untreated rectal cancer. However, the crater of the tumor, which had not been shielded from the hot water by the bag, was covered with an adherent brown slough, and the rolled edge of the lower two thirds of the tumor had vanished so that the soft, normal-looking mucosa ended abruptly in the slough-covered crater.

The only damage to the rectal mucosa was in a strip 8 mm. wide and 4 cm. long located at the level of the center of the tumor where there was superficial loss of mucosa, resembling a burn. Although the mucosa of the rest of the rectum had been exposed to the same amount of heat as the tumor, it appeared normal.

Histologically the thermal injury in the strip of damaged mucosa was limited to the mucosa. The rest of the heat-treated mucosa was indistinguishable from the untreated mucosa above the Foley bag. Histologic examination of the various heat-treated parts of the tumor showed only an occasional tumor cell deep in the fibrous tissue; whereas, the untreated part was typical of rectal cancer.

These observations and those reported in the first part of the century,[4,5] suggest that some cancers in man have a spectrum of heat sensitivity similar to that of cancers in mice and rats. It is therefore likely that heat could be used as a valuable adjunct to the treatment of cancer, especially when it is employed in conjunction with radiation.

Conclusions

The results of studies reported in the first 30 years of the century have been confirmed by our own observations, and suggest the following conclusions.

1. Some cancers, in both man and animals, are more susceptible to destruction by heat than are the tissues they grow in.

2. Heat acts synergistically with radiation in controlling the growth of many cancers.

3. The mechanism by which heat kills cells is poorly understood and deserves further study.

4. The uses of heat as an adjunct to the treatment of human cancers should be explored.

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RIGHT COLON USED AS AN ESOPHAGEAL PROSTHESIS

Report of Five Cases

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Department of General Surgery

A large part of esophageal surgery is concerned with restoration of a relatively normal function of swallowing by substituting other organs for the esophagus. Historical review of this surgery offers a fascinating chapter on technical ingenuity and daring,[1-3] but it is beyond the scope of this paper. In general, the evolution of surgical technics has led to the use of the mobilized stomach as the esophageal substitute of choice.

In the surgical treatment of carcinoma of the esophagus the primary mission is to perform the best cancer operation possible, and, secondarily to re-establish gastrointestinal continuity quickly and safely. To accomplish the second goal, there is no substitute for the stomach. A complete cancer operation in the thoracic esophagus involves the mobilization and resection of the principal areas of lymphatic drainage, most important of which is the chain of nodes reaching down along the left gastric vessels to the superior border of the pancreas. When this has been accomplished, mobilization of the stomach is approximately one half achieved and it is easy to complete the procedure.

Most patients adjust satisfactorily to the thoracic stomach created for the above-described purpose, particularly if a pyloroplasty is performed. However, there are other conditions, usually occurring in young patients, frequently involving most of or upper portions of the esophagus, and all of a benign cause, in which other approaches to the problem offer at least theoretic advantages. Hopefully, these lesions are associated with a normal life span, and the reservoir and digestive functions of the stomach presumably operate best in a normal anatomic situation. Also, there are certain well-known peptic difficulties associated with a thoracic position of the stomach and esophagogastric anastomoses, although their magnitude (particularly if a pyloroplasty has been performed), is probably overemphasized.

Efforts to use intestinal segments as esophageal substitutes in various planes, from under the skin on the anterior chest wall to the normal esophageal bed, have been employed for many years.[2,3] It has evolved that the right colon nourished by the middle colic vessels is optimal for esophageal substitution. Firstly, its vascular pattern is relatively constant, and secondly, the distance from the origin of the middle colic vessels to the tip of the cecum is roughly comparable to

the distance from the origin of the middle colic vessels to the suprasternal notch, so that when the right half of the colon is mobilized and rotated 180 degrees, the cecum will reach into the neck. At the other end there is no problem in approximating the transverse colon to the stomach. Another advantage in using a segment of colon in this manner for the replacement of benign esophageal disease is that the diseased esophagus may be abandoned in situ, and the colon may be passed up through an anterior mediastinal tunnel into a neck incision with no necessity for performing a thoracotomy.

We make no claims for originality in developing these technics,[4,5] and our experience to date, which is cited below, is extremely limited; however, the results have been so gratifying, both to us and to the patients, that it is thought worthwhile to present them here.

Technic

Preparation of the patient for surgery includes two steps. The first of these is the obtaining of a satisfactory nutritional status. Long-standing dysphagia is often associated with obvious malnutrition. The solution to this problem may be the preliminary placement of a catheter gastrostomy that facilitates a forced feeding program. We consider a gastrostomy a mandatory part of this operative procedure, and there is no particular disadvantage to performing it as a preliminary stage if necessary. The other step in preparation concerns the colon. It must be as clean as possible before being utilized as a transplant. A low-residue diet for two or three days, followed by a cleansing dose of castor oil and a 24-hour program of neomycin sulfate administered orally are utilized. The day before operation, enemas are given until the returns are clear.

The abdomen is opened through a short right paramedian incision. The ileum is divided two inches from the ileocecal valve, and the distal section is excised from its mesentery to the cecum. The ileocolic artery and its branches to the cecum are thus preserved *(Fig. 1)*. The remaining stump of ileum is closed and is invaginated into the cecum. The proximal ileum is seen to be nourished by the terminal branches of the superior mesenteric artery *(Fig. 2)*. The right colon is then completely mobilized from its bed and from its peritoneal attachments until it has been reflected medially from the second and third portions of the duodenum and from the head of the pancreas. The ileocolic artery and vein are divided as close to the superior mesenteric artery as possible *(Fig. 1)*. The proximal transverse colon is separated from the gastrocolic ligament and from the omentum. The right colic artery and vein (if present) are divided at their origin from the superior mesenteric vessels. The transverse colon is then divided between the primary divisions of the middle colic artery, if this vessel divides in the substance of the pancreas; or to the left of the middle colic artery, if the division point is near the mesenteric border of the transverse colon. The mobilized right colon must

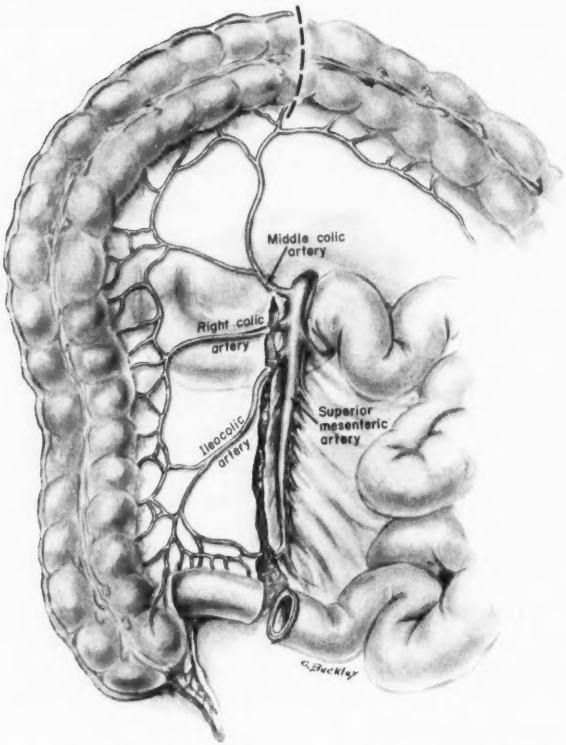

Fig. 1. Structures severed in mobilization of the right colon for esophageal substitution. The ileocolic and right colic arteries are divided at their respective origins.

swing freely on the pedicle of the middle colic artery, and must be completely separated from the head of the pancreas, the stomach, and the right renal area. A heavy silk ligature is tied around the appendix, and the ligature is utilized for traction while the cecum is pulled up posterior to the antrum of the stomach. The entire right colon is then pulled up until it lies above the lesser curvature of the stomach *(Fig. 3)*.

We believe it is important to pass the colon and its vascular pedicle posterior to the antrum of the stomach (rather than anterior to the antrum), for this maneuver gives significant additional length and also avoids the theoretic hazard that might be associated with gastric dilatation, stretching, and obstructing the middle colic vessels *(Fig. 4)*. Intestinal continuity is next re-established by an appropriate anastomosis between the ileum and the distal transverse colon.

At this point the anterior mediastinal tunnel should be prepared for the colon,

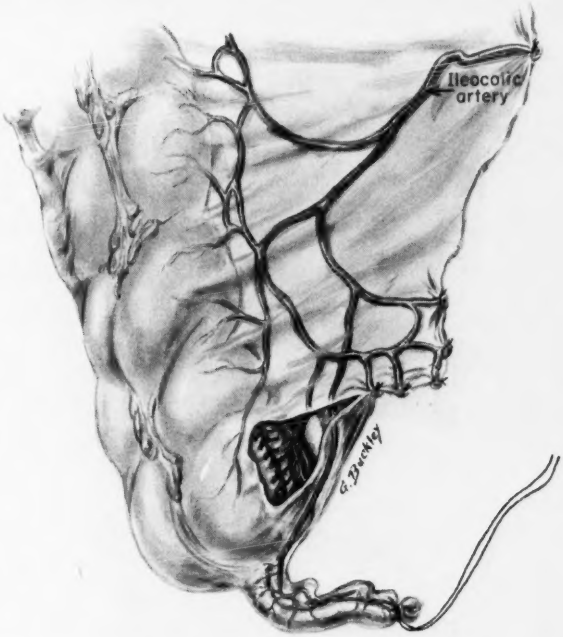

Fig. 2. Details of the ileocolic arterial supply after closure of the stump of the ileum, and invagination into the cecum. Note the preservation of the terminal branches to the cecum.

and the cervical esophagus should be mobilized for anastomosis to the cecum in the neck. The inferior portion of the tunnel is opened by breaking through into the anterior mediastinum with finger or blunt scissor dissection posterior to the xiphoid. The diaphragmatic attachments are not firm in this area and the maneuver is safe if care is taken to keep the dissection immediately on the posterior aspect of the sternum. By spreading the scissors, or by inserting two fingers and spreading them laterally, the size of the opening can be made as wide as necessary. Thus, access is gained to the anterior mediastinal plane between the sternum and the pericardium. It contains areolar tissue and is easily opened. The right pleural sac extends a varying distance over the pericardium into the mid-mediastinal region. Ordinarily it is not entered, but inadvertently an opening may be made. This is not harmful, but the possibility of a postoperative pneumothorax should be considered.

The optimal cervical exposure is obtained through an anterior sternocleidomastoid incision that commences at the sternal notch and extends approximately two thirds of the way to the mastoid process. Customarily we make this incision

Fig. 3. Position of the right colon after it has been pulled up into the mediastinum posterior to the gastric antrum.

on the left side. As at the lower end, the areolar space posterior to the sternum is readily entered with finger dissection. Once again, care should be taken to stay immediately posterior to the sternum, thereby avoiding the innominate veins. There may be some rather tough fascial bands restricting the lateral extent of this opening; these may be cut with impunity. In a child, a finger from above and below may readily be approximated posterior to the sternum; in an adult the distance may be too great, and a long instrument may have to be passed through the mediastinal tunnel and then be withdrawn in an opened position to obtain the necessary tunnel diameter.

In dissecting down to the cervical esophagus medial to the carotid sheath, the only structures that ever need to be sacrificed are the omohyoid muscle and the inferior thyroid vessels. The cervical esophagus is identified below the larynx and is mobilized throughout its circumference. Care should be taken to avoid the recurrent laryngeal nerves. An umbilical tape is placed about the cervical esoph-

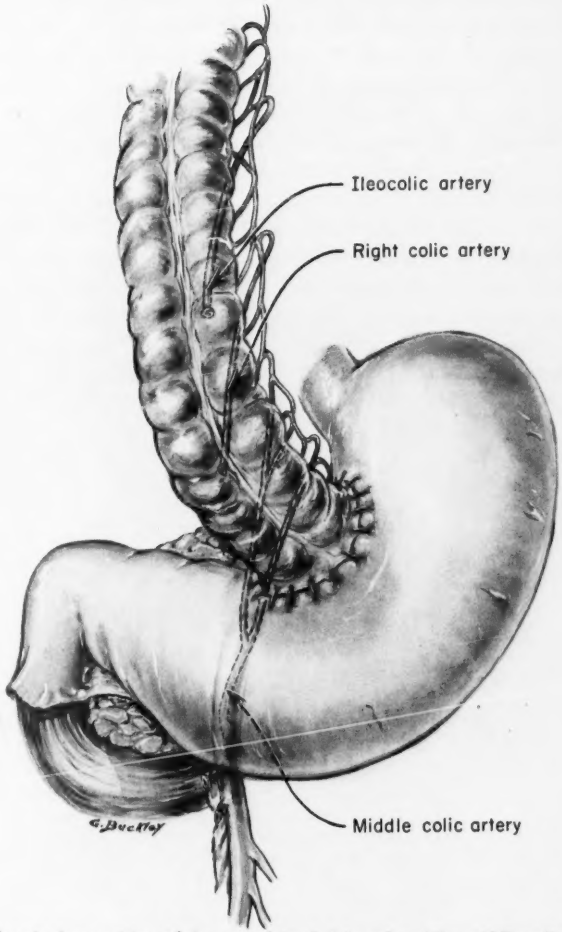

Fig. 4. The functioning position of the transplanted right colon. The middle colic artery pedicle lies posterior to the stomach.

agus and dissection is carried down around the esophagus as far into the mediastinum as is conveniently feasible. At the lowest point of dissection the esophagus is firmly tied with a heavy silk ligature. It is then divided immediately proximal to this ligature. Customarily we have then reinforced the distal closure with a continuous atraumatic catgut purse string suture. The esophageal stump is dropped into the mediastinum. It has caused no difficulties. The suture attached to the appendix is then passed up through the tunnel and, with gentle traction from above

and pressure from below, the cecum is teased up through the tunnel until it appears at the suprasternal notch. Before this maneuver we have found it valuable in several of the children carefully to enucleate a sizable mass of mesenteric lymph nodes in the immediate proximity of the cecum. Great care should be taken so as not to jeopardize any of the blood supply. We have found that the bulk of these nodes may be great enough to impede the passage of the cecum through the anterior mediastinum. It may require a surprising amount of maneuvering and gentle traction to tease the cecum up into the neck. In the course of this process, the tension on the middle colic vessels in the abdomen should be carefully assessed. When the appendiceal stump becomes apparent in the neck, a routine appendectomy is performed. The appendiceal stump is not located near to the apex of the cecum, and we have selected an appropriate cecal pouch for anastomosis. The most direct approximation of the esophageal stump and the cecum may be facilitated by dividing some of the underlying strap muscles *(Fig. 5)*. There are no vital intervening structures. We have performed an open one-

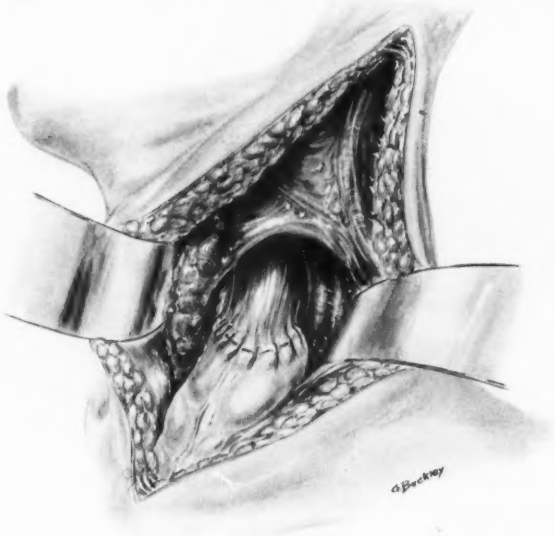

Fig. 5. Anatomic relationship of the esophageal anastomosis in the neck. The thyroid gland lies medial and the carotid sheath lateral to the anastomosis.

layer anastomosis using fine interrupted sutures with knots in the inside. It is important to place a small Penrose drain in the closure of this cervical incision in order that any possible leakage may be directed to the outside rather than toward the mediastinum.

Next, the abdominal portion of the operation is completed. The distal end of the colonic segment is tailored in length to be appropriately anastomosed, by an end-to-side interrupted technic, to the anterior wall of the stomach. There are then two additional important steps. The first of these is to create a catheter gastrostomy, bringing the catheter out through a stab wound to the left of the abdominal incision. This gastrostomy is vital for decompressive purposes, as it is not feasible to attempt to thread a Levin tube through the tortuous haustrations of the new colonic esophagus. After the need for decompression has passed, the tube may be used for feeding. We withhold oral feeding for the first postoperative week. The other operative step, which probably is important, is the construction of a pyloroplasty *(Fig. 6).* The colon — more than the esophagus —

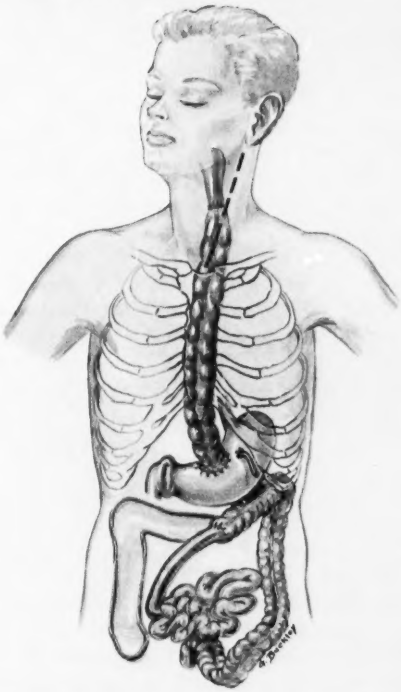

Fig. 6. Sketch of the completed operation. Pyloroplasty has been performed. The catheter gastrostomy is preserved. The ileocolic anastomosis has been completed.

seems to be resistant to peptic activity; nevertheless, we have routinely performed a pyloroplasty to minimize reflux.

Our total experience with this operation is next reported.

Case Reports

Case 1. A 26-month-old Negro girl was first examined by us in March, 1958. Ten months before examination she accidentally swallowed lye. An emergency tracheotomy was performed and a vigorous course of dilatations of the esophagus was instituted. However, dysphagia became progressively worse, and four months after the accident it was necessary to perform a feeding gastrostomy, after which time the dilatations were continued in retrograde fashion utilizing an indwelling string. The string was lost and a total esophageal atresia developed.

The physical examination here disclosed no remarkable findings. A tracheotomy and a gastrostomy were in place, and the child was obviously well nourished. As an initial procedure, two 5-mm. bronchoscopes were simultaneously passed down into the esophagus (through the mouth), and up into the terminal esophagus (through the gastrostomy). Using fine bougies it was impossible to find any channel whatsoever for a distance of about 4 cm. between the tips of the two bronchoscopes; in this fashion it was proved that there was total discontinuity of the esophageal lumen in the upper thoracic region.

The operative procedure with the technic just described was performed. The gastrostomy already in place was not disturbed, and the colon was implanted in the stomach distal to that point. The cervical portion of the procedure was not unduly complicated by the tracheotomy stoma, which was draped out of the field of the left anterior sternocleidomastoid incision.

The postoperative convalescence was uneventful. On the fourth postoperative day, it was apparent that she had learned to swallow saliva; previously she continually had to expectorate it. On the eighth postoperative day, she consumed applesauce with obvious pleasure. It was apparent, however, that swallowed matter caused distention of the cecal pouch that lay in the neck, indicative of hourglass narrowing of the colonic esophagus where it passed through the thoracic inlet; therefore, solid food was withheld for several days. Prior to discharge from the hospital she was eating a normal diet, with relish. There have been no difficulties, and the parents consider her a normal child, three years after the operation.

Comment. During her postoperative course in the hospital, the patient's swallowing resulted in distention of the cecal pouch, as mentioned, in a manner analogous to that of a chipmunk hoarding food in its cheek. This distention had completely disappeared two months postoperatively *(Fig. 7)*.

A surgical procedure of this type offered the only alternative to a permanent gastrostomy in this child. Total esophageal obstruction is extremely distressing to a patient because of the inability to cope with saliva by any means other than continuous drooling or expectoration. The small infant or the infirm patient may aspirate the saliva, and dire pulmonary consequences may ensue. It is gratifying to be able to cure a protracted and complicated disability of this type in a one-stage definitive operative procedure.

Case 2. A two-day-old infant girl was first examined in February, 1958, when she was referred to us because of a tracheoesophageal fistula. The diagnosis had been suspected when it was noted that the child regurgitated excessive amounts of mucus, and

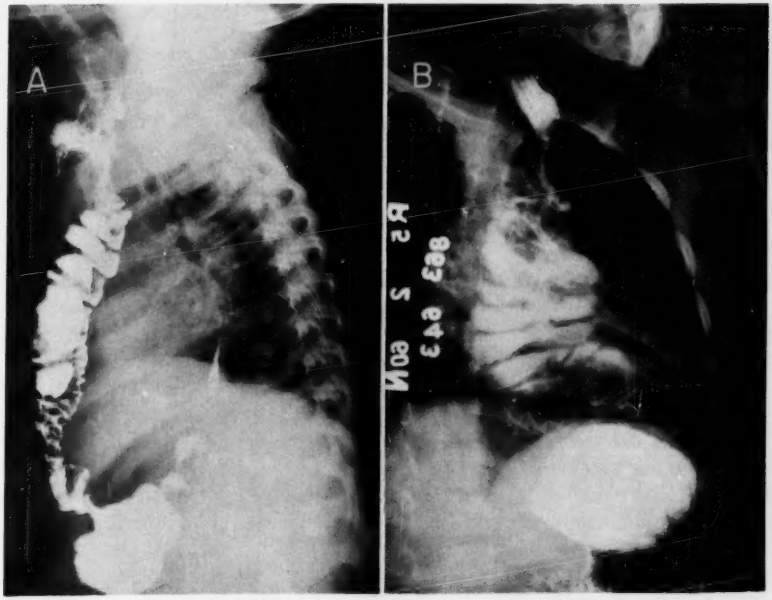

Fig. 7. Postoperative barium studies showing the function of the colonic esophagus. A, Demonstrates the immediate substernal location of the colon. Note the reflux of barium into the abandoned esophagus. This is a study on Case 1, a child with caustic stricture. The bottommost portion of the stricture is demonstrated by the barium reflux in the esophagus. B, Shows the extent to which the colon may dilate when exposed to negative intrathoracic pressure. This poses no clinical problem. Both of these views suggest that the sluggish colonic peristalsis plays only a small role in the swallowing function of these patients. Cineradiographic studies demonstrate that the barium cascades down through the colon by gravity.

it was confirmed by instillation of a small amount of Lipiodol* into the blind upper esophageal pouch. The terminal esophagus was proved to communicate with the tracheobronchial tree by the presence of air in the gastrointestinal tract.

The child was operated upon the next day. The blind proximal end was found to be extremely short, ending rather high up in the neck. The terminal esophagus arose from the inferior aspect of the carina. This fistula was taken down and closed; however, it was found that the two esophageal ends could not be approximated. The distal end was therefore tied, and the chest was closed. A feeding gastrostomy was constructed, and the cervical esophagus was exteriorized in the neck as a mucous fistula. It was decided to postpone reconstruction for two years. The child progressed well and was readmitted as planned in May, 1960, and, after considerable nutritional preparation, colonic substitution was performed according to the technic described.

The early postoperative convalescence was uneventful. On the seventh postoperative

*E. Fougera & Co.

day, the child took the first oral feeding of her life, and drank liquids well. An indurated area developed in the cervical incision which discharged a small amount of purulent material and some gas bubbles indicative of a small fistula; however, it healed rapidly and has not been a problem. Six months after the operation a report from the parents indicates that the child has had no difficulty, and she eats a normal diet for her age. Her appetite is excellent.

Comment. This is the youngest and smallest (weight, 20 pounds) patient upon whom we have performed this operative procedure. The small size of the structures did not pose any unanticipated operative difficulties. The described operative procedure offers the ideal solution to problems of congenital esophageal atresia when a primary anastomosis cannot be performed. We do not know how early in life the operation can safely be performed, but it seemed reasonable to us to defer it for two years to allow the child to grow. We are not aware of experience of other surgeons with younger infants. At the initial operative procedure in the newborn it is vital to exteriorize the upper esophageal stump so that the infant can swallow rather than aspirate the saliva. The fistula must also be divided so that gastric contents cannot regurgitate into the tracheobronchial tree.

Case 3. A five and one-half year old boy was first examined here in July, 1959, because since the age of two years he had had episodes of hematemesis which required numerous blood transfusions. In addition there was a problem of mild dysphagia with episodes of regurgitation of recently ingested food. In spite of iron therapy, his blood hemoglobin content was said to be frequently as low as 8 gm. per 100 ml.

Roentgenograms of the esophagus and stomach were not remarkable except for evidence of an ill-defined area of moderate narrowing immediately below the level of the aortic arch *(Fig. 8).* Esophagoscopy demonstrated a definite stricture at this level, and the mucosa changed to readily bleeding granulation and scar tissue. The esophagoscope could not be passed beyond the stricture that was thought possibly to be an inflammatory response to a long-retained foreign body. Mucosal biopsy specimens showed only fibrinous suppurative exudate. A week later the procedure was repeated, but no additional information was obtained; once again an acute inflammatory process was encountered and free bleeding resulted from dilatation and attempts at biopsy. The precise nature of the lesion was extremely puzzling, and a thoracotomy was believed to be indicated.

A right exploratory thoracotomy was performed. The vascularity of the posterior mediastinum was much greater than normal about the esophagus. There were also present a number of succulent, inflammatory lymph nodes. The esophagus was notably enlarged and thickened; however, palpating up and down the esophagus revealed no obvious localized lesion. The esophagus was opened longitudinally at the anticipated level of pathologic change. The muscular wall was noted to be hypertrophied and fibrotic. An area of fusiform narrowing was seen. There was definitely no retained foreign body, or mediastinitis. Several rents in the mucosa in this region were thought to be related to the previous instrumentation. Numerous mucosal biopsy specimens were removed. The reason for the bleeding was not apparent, and it was believed that, in view of the puzzling nature of the problem, a radical resection was contraindicated. The esophagus was reconstructed. The mucosal biopsy specimens showed chronic inflammation, necrosis, and suppuration, but no residual mucosa. The problem was basically

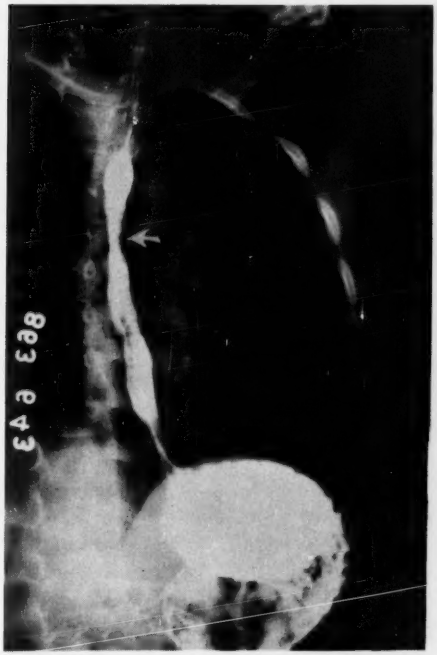

Fig. 8. Case 3. Preoperative barium study. The arrow indicates the area of stricture. In this area, a biopsy specimen of suppurative inflammation was obtained through the esophagoscope and free bleeding was seen. The mucosa below this area was proved to be gastric mucosa.

unchanged by this operative procedure although the tendency to bleed and to become anemic seemed to be somewhat less than preoperatively.

In February, 1960, the patient was again examined with a small esophagoscope. It was possible for the first time to pass the instrument beyond the area of narrowing into the lower esophagus. Biopsy specimens were removed at approximately the junction of the middle and the lower third of the esophagus, and these specimens consisted of gastric mucosa. The visual and radiologic anatomy at these levels was definitely esophageal, ruling out hiatus hernia and establishing the diagnosis of ectopic gastric mucosa.

In view of the almost life-long history of bleeding and stricture, it was decided that the most logical treatment was the operation under discussion. Postoperative convalescence was completely uneventful, and the boy was eating a normal diet at the time of discharge from the hospital. One year after operation there is slight difficulty only in swallowing lettuce and leafy vegetables. We wondered whether the functionless bypassed esophagus might still bleed. This has not been a problem to date and his blood hemoglobin content is now in the normal range.

Comment. The presence of ectopic gastric mucosa in the esophagus is extremely rare. Presumably the mucosa secretes in response to the same stimuli that cause normal gastric secretions, and results in peptic ulceration in the squamous mucosa above. This was the cause of the stricture and repeated bleeding in this patient. As an alternative procedure in this case, vagotomy and a gastric drainage operation were suggested. One wonders if the ectopic mucosa would not still secrete acid peptic juice when the level of division of the vagus nerves is further down the esophagus than the level of the ectopic mucosa, as would be the case with the conventional vagotomy. It was thought that in view of the severe fibrosis already present in the esophagus of the child at six years of age, although the stricture was not extremely severe, the most definitive action in regard to the many years ahead was to abandon his defective esophagus and construct a new one. Presumably the bypassed esophagus is still subject to its normal secretory stimuli; however, as stated, to date we have seen no evidence of further bleeding. We have seen this type of lesion in only one other patient, a middle-aged man. His problem was one of stricture without bleeding. He underwent vagotomy (transabdominal) and pyloroplasty; results were indifferent.

Case 4. A 43-year-old woman was first examined by us in March, 1960. Six months before examination, because of atypical cervical cytologic findings she underwent a hysterectomy. Malignancy was not confirmed on histologic examination. Two days postoperatively, some coffee-ground vomitus was noted, and gastric suction via a Levin tube was maintained for two days. Roentgenograms at that time are said to have shown an active duodenal ulcer. She was discharged from the hospital approximately 10 days after the operation; however, progressive dysphagia became a problem and she was rehospitalized one month postoperatively because of essentially complete esophageal obstruction. Roentgenograms at that time showed evidence of narrowing of the esophagus from approximately the level of the aortic arch on down. An esophagoscopic examination is said to have shown fiery-red mucosa at the upper end of this area. The mucosa bled readily.

A gastrostomy was performed for feeding purposes, and retrograde dilatations were commenced. In addition, she was maintained on steroid therapy for its antiinflammatory action. In spite of this program and in spite of the ability to dilate the esophagus repeatedly up to size no. 32 French the process did not abate. In view of the intractability of her bizarre esophagitis, she was referred to us for consideration of fabrication of a substitute esophagus.

Preparations were made for colonic replacement, which was performed in the manner described. Once again, the original gastrostomy was not disturbed. It should be mentioned that at the time of performing the pyloroplasty, no significant duodenal pathologic change was noted. On the sixth postoperative day the patient was first given a liquid oral feeding. At this time some induration of the cervical incision was noted. On the eighth postoperative day a definite fistula developed, from the anastomosis through the wound. Within six days the fistula closed spontaneously, and at the time of discharge from the hospital, the patient was eating a normal diet without any difficulty for the first time since she had undergone the hysterectomy.

The patient reported that six months after the operation she could swallow any food she desired, but was apt to have some indigestion from other than simple bland

foods. She noted that she sustained a feeling of fullness rather rapidly; presumably this is because of slow peristalsis in the colonic esophagus. However, she has been most happy not to be bothered with the gastrostomy tube and associated inconveniences, and stated that she would highly recommend the operation to anyone in her former predicament.

Comment. We do not understand the cause of this pernicious type of postoperative esophagitis; fortunately it is exceedingly rare. It is difficult to incriminate the Levin tube, as it was used for only 48 hours. Whatever the reason, it seemed to us that this patient had had a sufficiently long trial (six months) of vigorous treatment to combat the tendency to stricture, without significant success, and that definitive surgical correction was indicated.

Case 5. A Negro woman aged 33 years was examined in June, 1960, because of four days of total dysphagia that occurred acutely while she was eating chicken. She weighed 82 pounds, and gave a history of inability to swallow normally since childhood. Although she had no knowledge of possible ingestion of a caustic, it is presumed that this was the origin of the obstruction. Over the years, this patient had had multiple

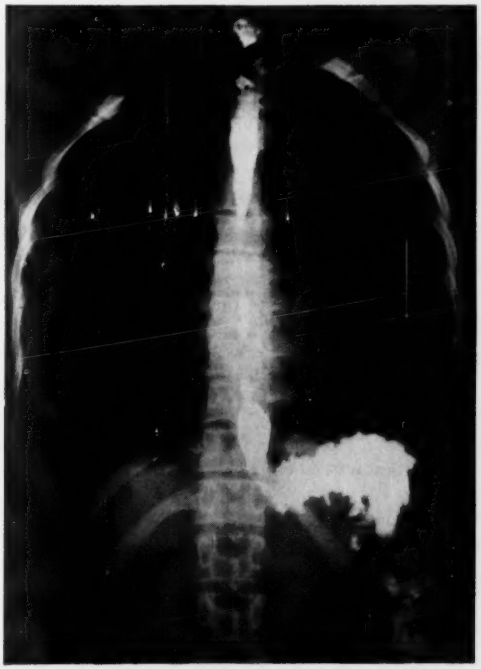

Fig. 9. Case 5. Preoperative barium study. The patient had long-standing multiple strictures presumably from caustic origin. Note that the topmost stricture is at the level of the first thoracic vertebra, and that there are several additional strictures lower down.

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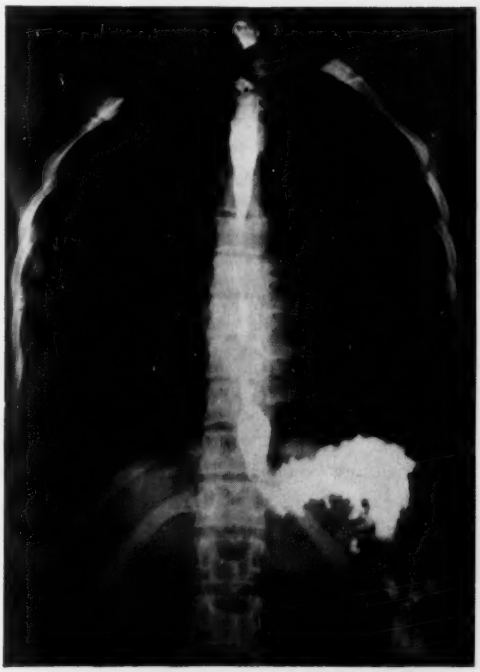

Fig. 9. Case 5. Preoperative barium study. The patient had long-standing multiple strictures presumably from caustic origin. Note that the topmost stricture is at the level of the first thoracic vertebra, and that there are several additional strictures lower down.

dilatations and had subsisted on a semiliquid diet. On one occasion, total dysphagia was precipitated by a watermelon seed.

She was examined with the esophagoscope, and the highest stricture was encountered at the level of the thoracic inlet *(Fig. 9)*. Bougies passed beyond this point encountered multiple narrowed areas. At the same time through a small laparotomy incision a catheter feeding gastrostomy was constructed. The patient eagerly accepted the idea of a colonic esophagus and the operative procedure described was performed. Recovery was uneventful, and six months postoperatively she reported that she gained 15 pounds and swallows normally. She stated that she is satisfied with the results of the operation and is glad that it was performed. She described some unusual sensations, such as a feeling that food seems to descend in a round-about way, and she frequently notes gurgling in the chest associated with swallowing.

Comment. This patient had lived with severe esophageal strictures for many years, and her condition was quite stable with dilatations being performed at only rather long intervals. The maximum-sized dilator that could be passed was a no. 26 French. It is pertinent that when an alternative to the prospects of a permanently restricted oral intake was offered, the patient eagerly accepted surgery.

Conclusion

The previous case reports require no further amplification. If one restricts the use of this operative procedure (substituting a segment of the right colon for the obstructed esophagus) to patients with nonmalignant esophageal problems, this becomes an operation of only sporadic usefulness. Caustic esophageal strictures today seem to be extremely rare, attesting to at least some effectiveness of parental education programs as well as the almost universal use of store-bought soap. However, in the occasional suitable patient, the described approach offers a dramatic one-stage cure in the person whose life will otherwise be burdened with a permanent gastrostomy or an interminable series of dilatations. To date, after performing five such operations, we are fortunate in having only satisfied patients.

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PERMISSION FOR AUTOPSY—GRANTED*

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AUTOPSY is one of medicine's most effective means to unveil medical mysteries. In the nineteenth century, for example, "generalized inflammation of the bowel" was a frequent cause of death. The precise nature of this disease was defined from the results of 446 autopsies, so that by the twentieth century the acutely inflamed appendix was removed before the onset of dangerous peritonitis.[1] Untold millions of persons owe their lives to the relatives of the deceased patients who allowed those investigations to be made.

Insulin was discovered through the study of tissues obtained at autopsy. Degenerating islets of Langerhans were found in the pancreas of a patient dead of diabetes. In 1921, insulin was isolated[2] from islets of Langerhans, and as a result today in the United States alone more than one million diabetic persons are able to lead relatively normal lives.

The primary purpose of an autopsy is to learn facts that will prevent the deaths of other persons having the same or similar conditions. To conduct an autopsy, legal permission must be obtained. To secure permission, a few facts, a little effort, and a deep personal belief in the good to be gained are all that are needed.[3] During the past year there were 45 deaths on our service and 44 autopsies were conducted. How we secured permission to perform those autopsies, and what information was particularly instructive, form the basis of this paper.

Securing Permission for Autopsy

The frequency with which permission is secured for an autopsy depends greatly on the attitude of the physician who requests it. The physician who has been closest to the family should always ask the permission. In keeping the relatives informed of the patient's progress, he has thoroughly established rapport, and is best suited to request the autopsy. Whether on duty or not, the resident physician who knows the relatives best, should be available if the patient dies.

Permission should be requested at the very time the family is told of death. Despite grief and shock, the average person will be more ready for reasonable discussion at that point than later. The request should be made in private to one person, the responsible relative.[4] The longer the interval after death, the less is the likelihood of the responsible relative's granting permission.

**This paper is from an essay that received First Prize in the Resident Essay Contest of the Ohio Chapter of the American College of Surgeons, September 9, 1960, in Akron, Ohio; and was prepared under the guidance and with the sponsorship of W. James Gardner, M.D., Head of the Department of Neurological Surgery.*

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The approach for the permission is determined by the type of individual the responsible person appears to be. There are three types of relatives easy to identify. Those most likely to give permission are the intelligent and informed. They need only reassurance and perhaps a logical explanation. Telling such a relative that everything possible was done to save the patient is all that is usually necessary to secure his permission. In other instances one may suggest that the death could have been the result of some inherited weakness, and that the examination might spare the life of some other member of the family.[5] The more intelligent the relative, the more will he appreciate the fact that the autopsy makes a contribution to medical knowledge.

A second type is the hysterical relatives. They are exceedingly difficult to approach. Here, kindness and understanding of their personal loss are needed. A young or hysterical mother may not be interested in the advancement of science as such, but she may be eager to do something that might spare another mother similar grief. If the person is unable to enter into a rational discussion, a sedative is indicated; the discussion then should be postponed until after a period of rest.

A third type includes those persons who are uninformed and of limited intelligence. They may have emotional problems that will complicate the physician's approach for a request for autopsy. For this group the explanation must be simple and brief. They may need to be told that the autopsy will cost them no money. A firm approach will frequently help secure the autopsy permission. The uninformed relative must be shown that signing the permit constitutes a legal responsibility and, at the same time, is a privilege.

The most common argument for refusal is that the deceased "has suffered enough." This argument is overcome by reassurance that the beloved one is in the hands of God, and what remains cannot suffer. Another reason is the unendurable thought of having the body cut into. A sympathetic explanation will emphasize that the examination is indeed like an operation, and that it will not affect the body for viewing at the funeral. A third reason for refusal is the question of possible violation of religious customs. A leader from the involved denomination when called upon will answer this question negatively. A fourth cause for refusal is the unwillingness to have students practice surgery on the deceased loved one. This misconception is corrected by assurance that only trained pathologists may carry out the examination. The fatalistic argument may be a stumbling block—that the inevitable outcome has occurred, and that the autopsy can serve no useful purpose; this can best be answered by comparing the purpose and the procedure of an autopsy to that of the routine physical examination of a living person.[6] For example, a routine physical examination could disclose an unsuspected tumor, or heart disease, which if treated immediately, could prevent serious subsequences.

Permission for autopsy can never be requested in a standardized manner; a

high rate of refusal follows such a stereotyped attempt. The approach must be humane, intelligent, and designed to fit the specific person who must be the one to give permission for autopsy. As outlined by Jeffers[7] there are several "don'ts" that are important: Don't appear to be apologetic. Don't allow irrelevant discussion. Don't overpersist. Don't compare the postmortem examination with embalming. Don't use the word "autopsy;" but say "complete examination" or "examination after death." The person responsible can be made to realize that his permission is needed in order to perform an autopsy, without the actual use of the word "autopsy" which sometimes is unpleasantly received.

On the neurosurgical service there is a policy of cooperation and support: if the resident who is making the request for autopsy is failing in the attempt, he should immediately stop the discussion and advise the senior resident or the staff physician, so that one of them may take his place. If the last physician who makes the request also is unsuccessful in his attempt, there still is an argument that may persuade. Forcefully remind the relatives that their beloved one is dead and the doctors have failed. Show them that doctors can do no better for the next patient with the same disease if nothing can be learned. But something can be learned if an examination is performed.

Autopsy permission was not granted in one case. This patient had not undergone an operation and was transferred, to our service, only for terminal care. The wife did not speak English and was unable to come to the hospital because she herself had heart disease. Furthermore, the physician belatedly met the stepdaughter, the next of kin, who subsequently refused permission.

Illustrative Cases

The autopsies disclosed unexpected findings in several cases. Five such cases are presented, two of which brought improvement to our present technics.

Case 1. A man was thought to have an intracranial hematoma. The night before he was scheduled for surgery, he suddenly died. The resident staff believed that an intracranial procedure had been delayed too long. Autopsy disclosed an unsuspected dissecting thoracic aneurysm as the cause of death.

Case 2. A woman fell the day after operation for trigeminal neuralgia. She was found unconscious with fixed pupils and was immediately taken to the operating room where the wound was reopened. When no intracranial hematoma was seen, a clinical diagnosis of brain-stem thrombosis was made. She died a few weeks later. The autopsy revealed that the cause of death was a subdural hematoma located a few centimeters above the upper edge of the operative wound.

Case 3. A woman had a subarachnoid hemorrhage. Findings on bilateral carotid and right vertebral arteriograms were normal. On the day of her discharge, another subarachnoid hemorrhage occurred and she died. Autopsy revealed an aneurysm on the only major intracranial artery that had not been visualized: the small segment from the contralateral vertebral artery. A bilateral vertebral arteriogram, which was never per-

formed as a standard procedure, would have established the correct diagnosis. Now, when a single vertebral arteriogram does not disclose the cause of a subarachnoid hemorrhage, a bilateral arteriogram is performed.

Case 4. A patient died after a decompressive laminectomy that had been otherwise uncomplicated. Coronary thrombosis was believed to be the cause of death. However, the autopsy revealed a massive air embolus. This initiated an investigation of similar previous complications. It disclosed that a light plane of anesthesia in a patient with an endotracheal tube was contributory to the complication of air embolus.

Case 5. A child had a huge cystic craniopharyngioma totally removed while under hypothermia. He tolerated the procedure well, but during the second postoperative week he died. At no time was there a fever; hence, the spinal fluid had not been examined. The autopsy revealed a severe widespread meningitis. The inflammatory process apparently had been concealed by the hypothermia.

Summary

In 44 of 45 cases, permission for autopsy was granted. Permission is obtained primarily on the basis of rapport previously established between the physician and the responsible person. The planned approach considers the responsible person's emotional and intellectual capacities so that the benefits of the postmortem examination will be understood by him. Unexpected findings in several autopsies brought about improvement both in diagnostic and in surgical technics.

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ABDOMINORECTAL PULL-THROUGH RESECTION FOR CANCER AND FOR HIRSCHSPRUNG'S DISEASE

Delayed Posterior Colorectal Anastomosis

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THE complications following conventional pull-through procedures for cancer of the mid-rectum or Hirschsprung's disease are certainly not to be minimized. Ischemic necrosis of the pulled-through segment, and retraction and abscesses in the presacral space are the most difficult complications to treat. Waugh and Turner[1] in summarizing their extensive experience and excellent results state that 13.4 per cent of their patients had some degree of slough and retraction of the pulled-through colon, while in 20.9 per cent infection developed in the presacral space.

We believe that ischemic necrosis, retraction, and presacral infection are due to: (1) the too frequent reliance on the sigmoid colon as the pulled-through segment, (2) insufficient external fixation of the exteriorized colonic segment, and (3) immediate replacement of a colorectal anastomosis into a compartmented pelvic hematoma (as in Swenson's operation). The technic reported here ensures the removal of the sigmoid colon (which occasionally is of doubtful viability after mobilization), adequate and absolute fixation of the exteriorized colonic segment on the perineum, and a safe, delayed colorectal anastomosis after the incubation period of pelvic abscess is past, or the infection, if present, has been controlled.

The delayed anastomosis technic described here was evolved by us in 1952 for adults having small cancers located in the mid-rectum, and in whom a Swenson type[2] of pull-through resection was performed. In 1953, we utilized the same technic in children undergoing resections for Hirschsprung's disease. In September, 1960, in Sao Paulo, Brazil, one of us (R.B.T.) was pleased to note that Dr. Daher E. Cutait[3] had independently utilized the delayed anastomosis in adults who had undergone pull-through resections for the acquired megacolon of Chagas' disease.

Technic of Pull-Through Resection of the Rectum and the Sigmoid Colon

Abdominal phase. The sigmoid colon is mobilized and the mesentery is stripped medially from the left ureter, iliac vessels, and aorta up to the third portion of the duodenum where the inferior mesenteric artery and vein, and left colic artery,

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are ligated and are divided. The rectum is freed from its pelvic attachments as in the Miles's[4] operation except that the distal dissection is carried on through the levatores ani. Two stout braided silk ties are placed around the rectum two inches below the neoplasm; another is placed just above it. (The lumen of the bowel is thoroughly washed with a cancerocidal solution.) At this juncture, a pull-through operation requires that the entire left colon and splenic flexure mesentery be mobilized and be detached from the lower border of the pancreas above the ligament of Treitz. (The omentum is excised from the distal transverse colon.) The inferior mesenteric vein is again divided, this time at the ligament of Treitz. The mid-sigmoid colon will now stretch to the mid-thigh. The sigmoid-descending-colon junction is selected as the probable site for perineal resection of the left colon, and small arteries of the epiploic appendixes are cut in order to determine arterial flow. If pulsations are not seen, larger mesenteric vessels are divided near the colon until pulsation is obvious. (Note: Distally, the blood from cut sigmoid arteries flows but does not pulsate.) A heavy black braided silk tie is then placed as a marker. The bowel is not divided — thus protecting the presacral space from unnecessary contamination.

Perineal phase. In an exaggerated lithotomy position the anus is dilated; the lower ampulla (below the silk tie) is cleansed thoroughly and repeatedly with tincture of benzalkonium chloride.* If the anus is rigid and unyielding, the lower band of the internal sphincter is divided through a short radial incision in the anal skin of one of the posterior quadrants. The rectal mucosa above the dentate line is grasped with hemostats and is everted *(Fig. 1A),* and the rectum is completely severed through the mucosa about 1 cm. above the dentate line. The abdominal colorectal segment is gently pulled through the everted rectal stump until the black-silk marker at the sigmoid-descending-colon junction is in sight *(Fig. 1B).* The colon now lies directly over the aorta *(Fig. 1C),* the rectum and sigmoid portions having been withdrawn. The mesentery usually lies posteriorly at the anus. The protruding colon is severed about two inches from the anus; bleeding mesenteric vessels are ligated; and the short, everted rectal segment is sutured to the seromuscular layers of the protruding colon *(Fig. 2A).* The colonic segment is wrapped in folded gauze and is held in firm position by skin clips *(Fig 2, B and C)* to prevent retraction. The end of the colon is clipped to the gauze wrapping.

Completion; abdominal phase. The left colon mesenteric defect is obliterated by suturing the mesentery to the preaortic tissues, to prevent herniation of small intestine. The accumulated blood in the pelvis is removed by suction, and several large soft-rubber tissue drains are placed in the depths for pelvic drainage of the blood and serum. (The drains may be left in as long as necessary, because they do not lie against an anastomosis.) The pelvic peritoneum is not reconstructed.

**Zephiran chloride, Winthrop Laboratories.*

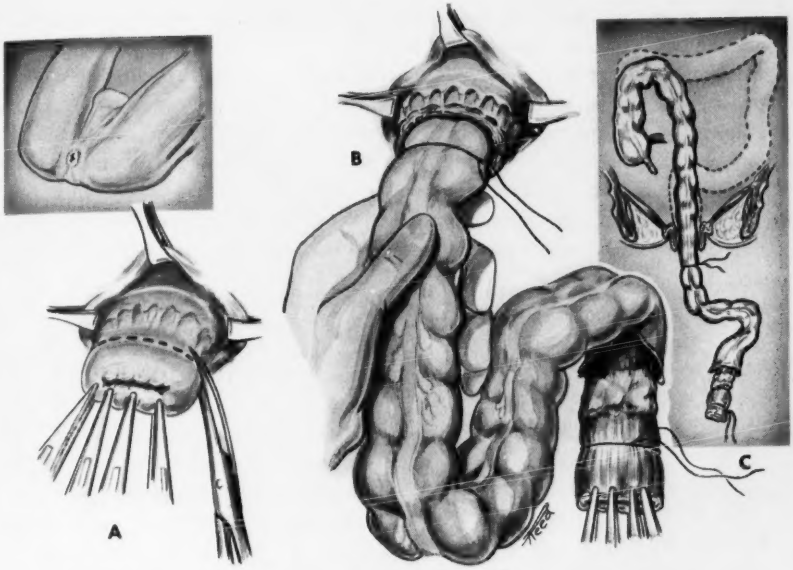

Fig. 1. Details of the perineal phase of a pull-through resection. A, Division of the slightly everted rectum. B, Pull-through of the rectum and sigmoid colon. C, Pull-through completed.

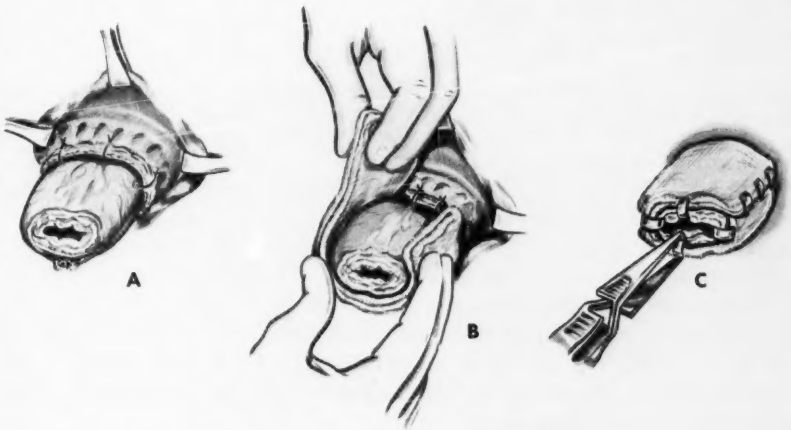

Fig. 2. Fixation of the colonic stump with a gauze stent and clips.

It is left open to allow free drainage of blood and serum into the abdominal cavity. The abdomen is closed.

Management of perineal colostomy. During the first ten postoperative days, the colon is lavaged daily by enema through the perineal colostomy. Ointments are used on the skin to prevent irritation. By the tenth or twelfth day, there is firm union between the colon and the everted rectal stump, and posterior resection with anastomosis can be performed *(Fig. 3).* If an abscess has developed in the presacral space, it can be drained alongside the protruding colon, and the space can be lavaged with a catheter. The posterior anastomosis can be delayed as long as necessary.

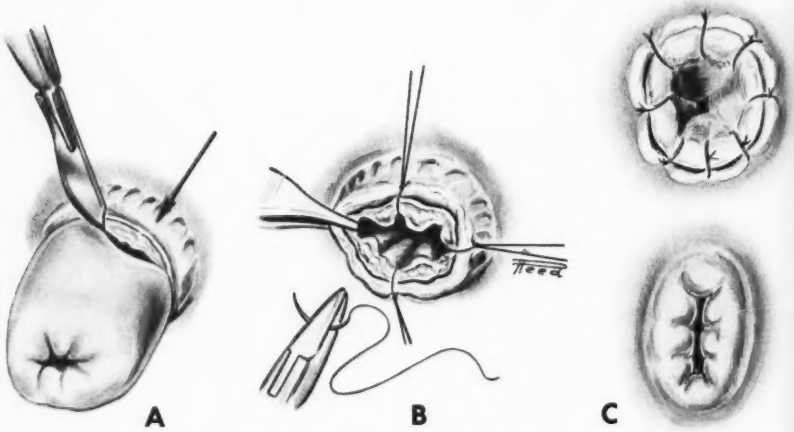

Fig. 3. Delayed (tenth day) perineal colorectal anastomosis. A, Resection of protruding colon. B, Full-thickness suture colorectal anastomosis. C, Completed anastomosis and retraction.

Figure 3 shows the details of the posterior anastomosis done on the tenth day. With the patient in left lateral position under caudal or local anesthesia the gauze collar is removed. The edematous colonic segment is cut off flush with the protecting everted rectal stump *(Fig. 3A,* arrow), and end-to-end anastomosis is made with 0000 chromic catgut through all layers. In adults, no more than 1 cm. of mucosal-covered rectum above the dentate line must be preserved, since a longer segment will not retract spontaneously after the anastomosis has been made. *Figure 3B* shows the placing of catgut sutures (by quadrants), the finished anastomosis, and the final spontaneous retraction that occurs within 24 hours. *Figure 4* shows the retracted anastomosis in position.

Bowel management. Although true continence is possible in some patients, the majority have many small movements and oozing of stool through the anus secondary to fecal accumulation. A one-quart daily enema will stop further move-

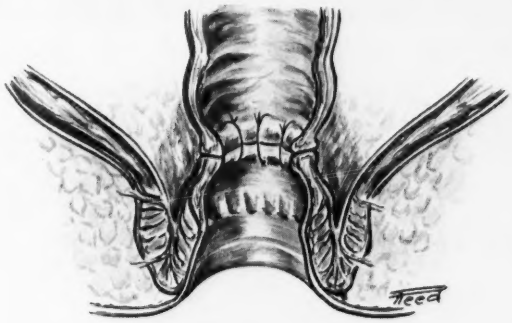

Fig. 4. Tenth-day anastomosis after retraction.

ments until the anastomotic area becomes soft and sensitive.

Management of presacral hematoma and abscess. Fever and leukocytosis during the 10-day period after operation may indicate infection of the presacral collection of blood. This can be drained by inserting a finger through the anus and into the space. Constant lavage through a catheter usually is effective. The final colorectal anastomosis can be delayed as long as necessary.

Results

Tables 1 and *2* list the complications that occurred in comparable groups of patients undergoing pull-through resections for cancer, Hirschsprung's megacolon, and other conditions from 1949 through 1960. The most serious complications occurred in the patients who had cancer. Although the comparisons

Table 1.—Immediate posterior anastomosis: *major complications that occurred in 36 patients after pull-through resection (1949-1960)*

Primary disease	Number of patients					
		Major complication				
	Total	Presacral abscess	Retraction	Slough	Leaking anastomosis	Postoperative death
Cancer	22	6	1	1*	2	2
Megacolon	12	1	0	0	0	0
Imperforate anus	2	0	0	0	0	0
Grand total	36	7	1	1	2	2

*Patient had had previous aortic resection for aneurysm.

Table 2.—Delayed posterior anastomosis: *major complications that occurred in 37 patients after pull-through resection (1949-1960)*

	Number of patients					
		Major complication				
Primary disease	Total	Presacral abscess	Retraction	Slough	Leaking anastomosis	Postoperative death
Cancer	23	3	0	0	0	0
Megacolon	7	1	0	0	0	0
Imperforate anus	3	0	0	0	0	0
Ulcerative colitis	1	1	0	0	0	0
Villous tumor	2	0	0	0	0	0
Radiation fistula	1	0	0	0	0	0
Grand total	37	5	0	0	0	0

between *Tables 1* and *2* may not be of statistical significance, there were no deaths from leaking anastomosis, no retraction of the pulled-through colon and fewer presacral abscesses in the delayed anastomosis group. Ischemic necrosis of the pulled-through colon *(Table 1)* occurred in a patient who previously had an aortic resection for an aneurysm. This low incidence is credited to the complete removal of the sigmoid colon with its unpredictable blood supply. The presacral abscesses were due to operative contamination of the collection of blood in the presacral space, and in each instance the rectum was either inadvertently opened during the pelvic dissection or was divided (technic of Swenson) before the pull-through procedure was accomplished; in two patients *(Table 1)* the anastomosis leaked after it had been completed and had been returned to the pelvis (immediate anastomosis).

Conclusion

A technic for delayed posterior colorectal anastomosis has been presented. The serious complications after this procedure have been fewer than those after primary colorectal or coloanal anastomoses. Anastomotic leaks are not possible. Should a presacral abscess develop, drainage can be effected through the anus, and colorectal anastomosis may be delayed as long as necessary. The technic is particularly adapted to pull-through resections in adults in whom a primary anastomosis of the Swenson type is difficult or impossible to perform because of rigid sphincters and perineal tissues.

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EVALUATION OF ERROR IN MEASUREMENT OF pH OF BLOOD AT ROOM TEMPERATURE

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BLOOD pH values obtained in vitro vary as inverse functions of the temperature of the specimen. These variations are sufficiently great that values determined on blood at room temperature must be corrected to have clinical significance. Ideally, measurements of blood pH should be made at body temperature, and the modern manufacture of instruments is now rapidly providing the means for such measurements. But many determinations are still made at room temperature, and then are corrected to yield what is presumed to be true in vivo pH values.

Rosenthal[1] as well as Craig, Lange, Oberman, and Carson[2] studied the effect of temperature on blood pH, and in each study a formula was derived that purported to allow accurate corrections to be made. These formulas are shown in *Table 1* in which pH_{37} and pH_{38} are the values at 37 and 38 C., respectively, and pH_t is the value observed at room temperature. Objections have been raised to

Table 1.—*Correction formulas for pH of human blood measured at room temperature*

Rosenthal[1]	$pH_{38} = pH_t\ (38_t)\ 0.0147$
Craig and associates[2]	$pH_{37} = pH_t\ (37_t)\ 0.0149$

this practice of measuring blood pH at room temperature and then correcting the observed values by means of one of the formulas. The objections are based on the possible variations in the responses of specimens from different persons to changes in temperature.[1-3] The total number of persons from whom specimens were obtained for examination in two independent studies[1,2] was only 46, which probably is insufficient to appraise the full potential error of the technic.

The work presented here involves blood specimens from 243 patients. The findings confirm the observations of other workers that individual variations occur, and furthermore they indicate the probable numerical error in correcting the pH of blood measured at room temperature.

Materials and Reagents

The blood specimens from 243 patients in the Cleveland Clinic Hospital were examined over an eight-month period. Two pH meters were used in this study. One was a Cambridge Research Model* with a micro glass electrode of the con-

*Cambridge Instrument Co., 3732 Grand Central Terminal, New York, New York.

denser type having a capacity of 0.4 ml. This instrument was used to measure blood at room temperature. The complete assembly is shown in *Figure 1.* The

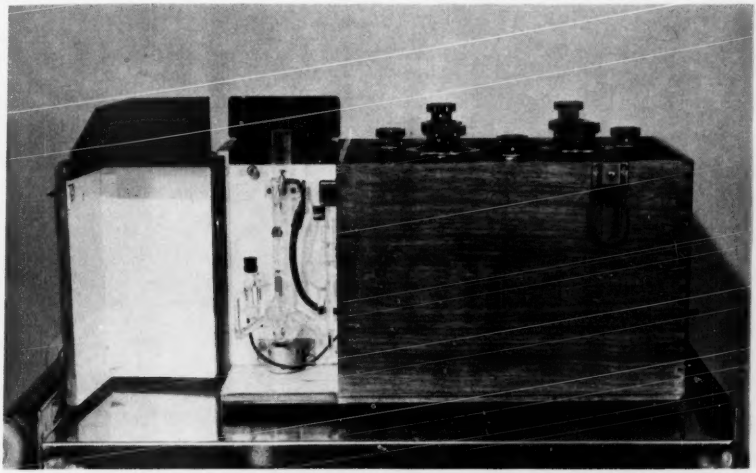

Fig. 1. Photograph of Cambridge Research Model pH meter.

other pH meter was a Metrohm Precision Compensator E322* using a Metrohm Blood Electrode, type EA 520, with a capacity of 0.05 ml. A Haake thermostat, type "F," was used to circulate water at 37.5 C. through the jacket of the glass electrode. Both instruments were standardized with phosphate buffer (0.025 M, pH 6.86 at 25 C., pH 6.84 at 37 C.) immediately before each series of measurements was made. *Figure 2* shows the complete apparatus.

Procedure

One glass bead, 1 ml. of mineral oil,† 2 drops of heparin sodium,‡ and 4 drops of 10 per cent sodium fluoride were placed in the barrel of each syringe. The plunger was fitted into the barrel, and with the tip pointed upward the excess oil was expelled; the tip was then wiped off and the syringe was capped. With the tourniquet in place, from 5 to 10 ml. of blood was withdrawn from the antecubital vein. The syringe was capped and the blood was mixed with the reagents. The measurements of pH were made directly from the syringe usually within one hour of collection. In rare instances, the sample was kept in the syringe and was stored in a refrigerator until it could be examined, at which time it was allowed to come to room temperature before the measurements were made.

C. A. Brinkman & Co., Inc., 115 Cutter Mill Road, Great Neck, Long Island, New York.
†Standard Oil Company of Ohio, light No. 135, NF grade.
‡Heparin sodium, 1000 USP units per milliliter, Organan, Inc., Orange, N. J.

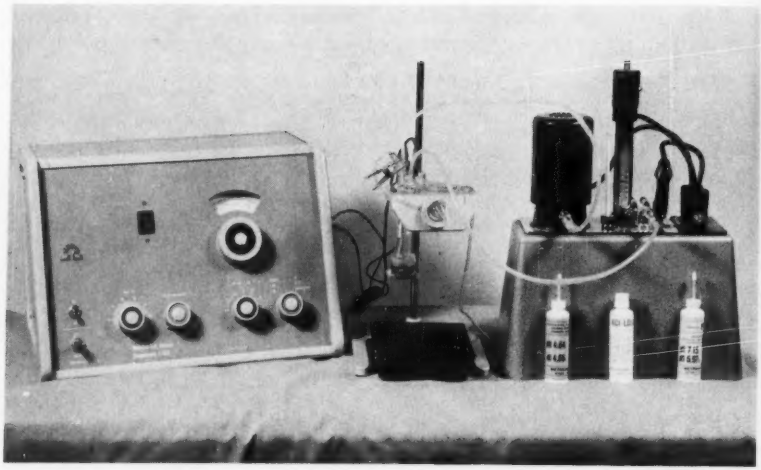

Fig. 2. Photograph of Metrohm pH meter with Sanz blood electrode and Haake thermostat.

Results

The deviations of the corrected blood pH values, from those on the same specimen at 37.5 C. are summarized in *Table 2. Figure 3* presents the findings graphically, and indicates that the deviations were almost equally distributed on either side of the zero point.

Table 2.—*Deviations in pH units of 243 human blood specimens: measured at room temperature and corrected to 38 C.,* measured at 37.5 C.*

Deviations, pH unit	Specimens		Cumulative percentage
	Number	Percentage of total	
±0.00	41	16.9	16.9
±0.01	84	34.5	51.5
±0.02	53	21.8	73.2
±0.03	39	16.0	89.3
±0.04	20	8.2	97.5
±0.05	3	1.2	98.7
±0.06	1	0.4	98.9
±0.07	1	0.4	99.0
±0.08	1	0.4	99.4

*Corrections made with Rosenthal's[1] formula *(Table 1)*.

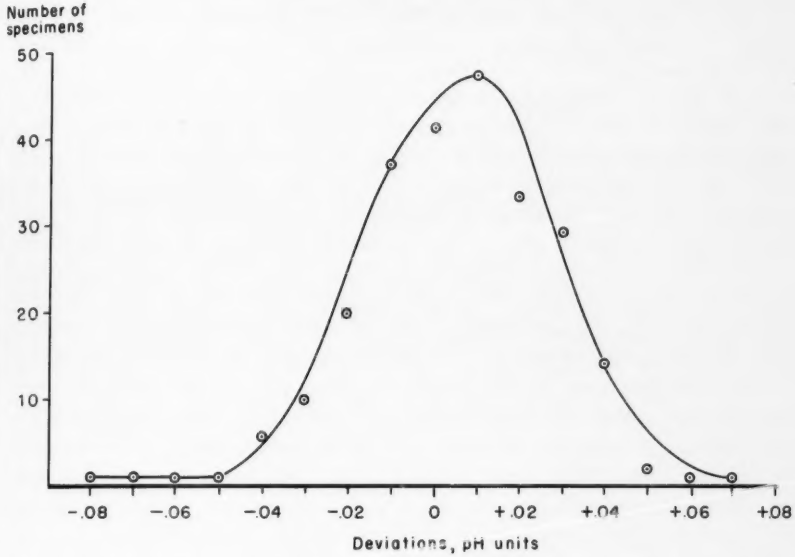

Fig. 3. Graph showing the deviations in pH units of the corrected blood pH values. Note that deviations are almost equally distributed on either side of zero.

Discussion

In Rosenthal's study,[1] pH values of blood specimens, from humans, measured at room temperature were compared with values on the same specimens at 38 C. His analyses were performed with semi micro glass electrodes. Three samples were determined simultaneously in three identical glass electrodes. The electrical potential of each glass electrode was measured with respect to the same calomel reference electrode in the same amplifying circuit. One aliquot of each specimen was maintained at 18 C., one at 38 C., and the third at some intermediate temperature. Rosenthal[1] found that the pH of blood was an inverse linear function of the temperature over the range from 38 to 18 C. He further observed that the slope of the line relating blood pH to temperature exhibited little variation among specimens when the initial values at 38 C. were from pH 7.25 to 7.45. From his data he calculated the mean temperature coefficient to be 0.0147 pH unit per degree, with a standard deviation of 0.006.

Craig and his associates[2] used Cambridge Research Model pH meters with condenser glass electrodes. The pH values of 27 blood specimens were compared under two sets of conditions. In the first study, each of 18 specimens was divided into two portions. One pH meter and one portion of the specimen were equilibrated at 37 C. and the portion of the specimen was measured. After the meter had cooled

to room temperature, it was used to measure the other portion of specimen. In order to exclude the possibility that the delay in reading one portion of the sample might have affected the pH, a second procedure was employed. One pH meter was equilibrated at 37 C. and the other at room temperature. Nine additional specimens were measured almost simultaneously with the two instruments. The temperature coefficient obtained in both studies was 0.0149 pH unit per degree with a standard deviation of 0.00273. Although this coefficient is essentially the same as Rosenthal's,[1] the standard deviation is somewhat greater. Craig and associates[2] called attention to the fact that of the 52 human specimens examined by Rosenthal,[1] 34 were from the same person; this factor may have reflected an unusually small standard deviation. Craig and associates[2] further stated that on the basis of their own coefficient and standard deviation, the maximal error in measuring the pH of any given blood specimen probably would not exceed 0.05 pH unit.

Since the over-all inaccuracy of the Cambridge pH meter[4] is about 0.02 of a pH unit, and the absolute accuracy of the Metrohm instrument[5] is 0.01 pH unit, the extent of the discrepancy of the measurement from purely instrumental causes could be as high as 0.03 unit if the errors were additive. It was assumed that when the two measurements were discrepant, the one at 37.5 C. was probably the more accurate of the two. Deviations from the result at 37.5 C. that exceed 0.03 unit can therefore logically be assigned to individual variations in the specimens from the average.

It is seen that errors of 0.05 pH unit or even higher may by incurred when measurements of pH are made at room temperature and the results are corrected by a standard formula. These errors may be either plus or minus, thereby doubling the uncertainty. For the greatest accuracy, pH measurements of blood should be made at the patient's actual body temperature. When this is not feasible, a satisfactory approach to the ideal is to measure the specimen at the usual average body temperature, 37.5 C. When measurements are made at room temperature, the possibility of large errors should be recognized, even when correction factors are applied.

Summary

In 243 patients, pH values of blood, measured at 37.5 C., were compared with the corresponding values determined at room temperature and were corrected by means of Rosenthal's[1] formula. Discrepancies of 0.05 pH unit and even higher were observed between the two sets of values. As much as 0.03 unit may be due solely to instrumental variation. It was assumed that the values at 37.5 C. were more nearly correct than those at room temperature and that deviations in excess of 0.03 pH units were errors due to variations in specimens.

Ideally, blood pH measurements should be made at the body temperature of the patient, but practically, measurements made at some standard temperature in the normal range, such as 37.5 C., are usually satisfactory. If this cannot be done, it should be recognized that errors of considerable magnitude may occur.

Acknowledgment

The author is grateful to Mr. Bradford Hale for technical assistance in this study.

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THE TREATMENT OF DIABETES INSIPIDUS WITH BENZYDROFLUMETHIAZIDE* AND POTASSIUM CHLORIDE IN ELEVEN PATIENTS

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REPORTS[1-5] of experimental treatment of diabetes insipidus with chlorothiazide and hydrochlorothiazide, and the more recent report[2] of the similar treatment of patients, prompted us to treat two patients, with this disease, with benzydroflumethiazide, a chlorothiazide-like drug.* Because hypokalemia was a problem reported by other investigators,[3,4] we used benzydroflumethiazide supplemented with potassium chloride. It was not our intention to make a detailed laboratory study to assess the results of treatment, but merely to assess its clinical effectiveness by means of pertinent simple laboratory tests that can be done on an outpatient basis.

The effects of the drug were ascertained in 11 patients with diabetes insipidus. In six of them there were definite favorable responses to the therapy. The 24-hour urinary volumes decreased from original values in the range of 4,000 to 10,000 ml. to between 2000 and 5000 ml. In two patients the urinary volumes decreased to approximately half the original values for a few days, and then increased again. In two other patients there were no responses at any time to the therapy. The results in the 11 patients are summarized in *Table 1.*

Illustrative Case Reports

Case 1. A 12-year-old white girl‡ was examined on August 20, 1960, because of symptoms of polydipsia and polyuria of 10 months' duration. Her birth, developmental, and family history were noncontributory. Her height was 60 inches and she weighed 109 pounds; blood pressure was 114/74 mm. of Hg; pulse rate, 84; the remainder of the physical examination disclosed no abnormality. The blood hemoglobin was 13.3 gm. per 100 ml.; cell volume was 42 per cent; leukocyte count, 8200 per cubic millimeter; fasting blood sugar, 68 mg. per 100 ml.; blood urea, 17 mg. per 100 ml. The serum electrolyte values were within normal limits. The 17-ketosteroids were 2.6 mg. per 24 hours; 17-hydroxycorticoids, 2.6 mg. per 24 hours; roentgenograms of the chest, skull, and sella turcica, normal; electroencephalogram, normal; visual fields and optic

**Naturetin with K, supplied through the courtesy of E. R. Squibb & Sons, 12655 Coit Road, Cleveland 8, Ohio.*

†Fellow in the Department of Pediatrics.

‡This patient was studied through the courtesy of Dr. R. P. Ostergaard, Warren, Ohio.

Table 1.—*Results of benzydroflumethiazide therapy in 11 patients with diabetes insipidus*

Cause of diabetes insipidus	Number of patients	Urinary volume, ml./24 hr.	
		Before therapy	After therapy
Chromophobe adenoma	2		
		5000	2500
		4000	2000
Hypophysectomy	3		
		4200	2000
		8000	2700
		5000	Same
Idiopathic diabetes insipidus	3		
		5500	3000
		10000	5000
		6300	2400 (failed later)
Sarcoidosis	1	8400	3200
Craniotomy	1	6500	2500 (failed later)
Craniopharyngioma	1	4000	Same
Total	11		

fundi, normal. Serial 24-hour urinary volumes were collected for seven days *(Fig. 1)* before treatment with benzydroflumethiazide, and ranged from 5500 to 6000 ml. with a specific gravity between 1.001 and 1.002. After three periods of fluid restriction for 12 hours, the specific gravity of the urine was 1.002 or less. A Carter-Robbins test was performed and was diagnostic of diabetes insipidus *(Fig. 2)*.

Case 2. A two and one-half year-old girl was first examined in December, 1958, because of a history of polydipsia and polyuria of 16 months' duration. At the onset of the symptoms, her family physician performed a therapeutic test with pitressin tannate. The patient received 1 ml. of pitressin tannate intramuscularly, and remained symptom-free for from four to seven days. Two weeks before examination here, she required one or two injections daily to maintain control of the polydipsia and polyuria. The birth, developmental, and family history were noncontributory. Her height was 38¼ inches and she weighed 31½ pounds; blood pressure was 90/60 mm. of Hg; pulse rate was 88. The physical examination disclosed no abnormality. The laboratory data were: blood hemoglobin, 12.9 gm. per 100 ml.; leukocyte count, 9000 per cubic millimeter; urinalysis, normal; roentgenograms of the chest, skull, and sella turcica, normal; serologic tests, normal; fasting blood sugar, 68 mg. per 100 ml.; serum electrolytes, normal; cerebrospinal fluid, 4 white blood cells, 19 mg. of protein; electroencephalogram, focal discharges originating from high brain stem area; pneumoencephalogram, normal; Carter-Robbins test, diagnostic of diabetes insipidus.

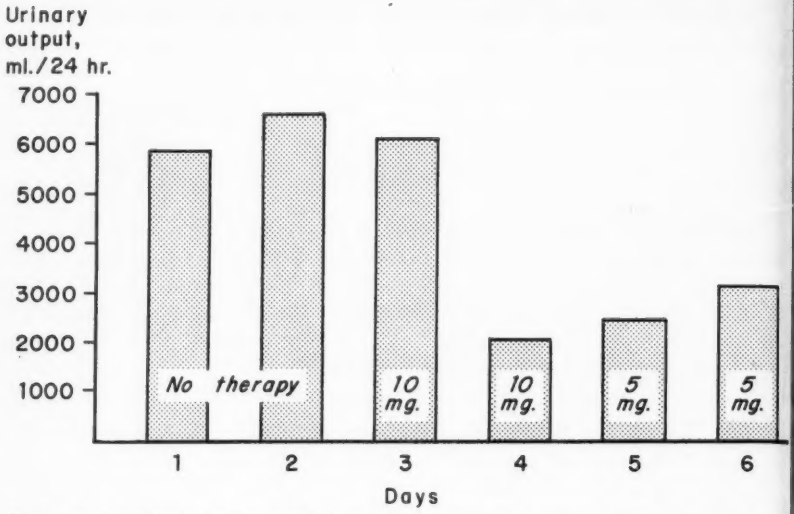

Fig. 1. Case 1. Graph showing the daily urinary volumes before and after treatment with benzydroflumethiazide in a 12-year-old girl.

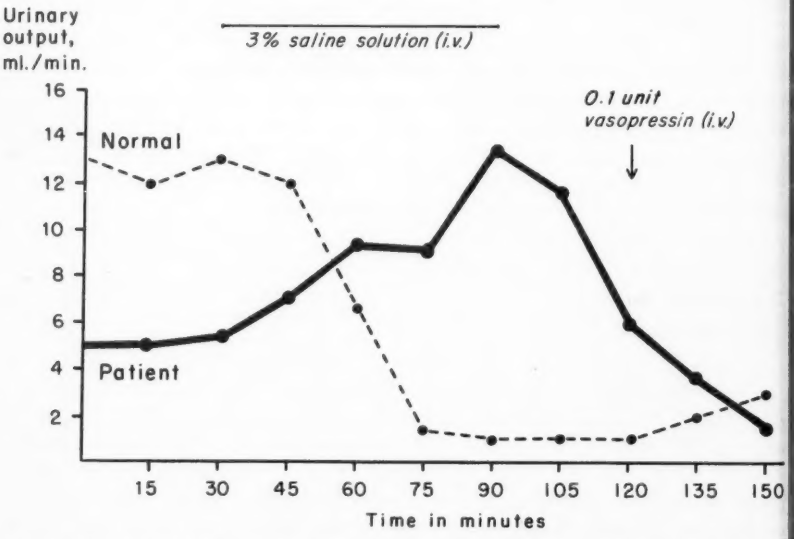

Fig 2. Case 1. Graph showing the minute-urinary volumes in a 12-year-old patient with diabetes insipidus, as compared with the normal volumes after intravenous injection of 3 per cent saline solution and vasopressin in a Carter-Robbins test in the patient.

Treatment consisted of injections of 1 ml. of pitressin tannate as required. She was maintained on this dosage for three months, requiring an injection every three or four days. The polydipsia and polyuria increased, and the dose was increased to 2 ml. of pitressin tannate. She remained asymptomatic on this treament for approximately six months, when the symptoms again became so severe as to require two injections daily for control. At that time a preliminary course of benzydroflumethiazide was begun, 5 mg. orally daily, and 1 ml. of pitressin tannate intramuscularly as required. On this regimen she required an injection every three or four days. She was readmitted to the hospital for re-evaluation and a trial on benzydroflumethiazide therapy alone. On admission her height was 43½ inches and she weighed 36 pounds. Blood pressure was 100/50 mm. of Hg; pulse rate, 80; the physical examination disclosed no abnormality. Laboratory data were: blood hemoglobin, 14 gm. per 100 ml.; white blood cells, 7500 per cubic millimeter; urine specific gravity, 1.003; blood urea, 15 mg. per 100 ml.; 17-ketosteroids, 5.6 mg. per 24 hours; 17-hydroxycorticoids, 2.1 mg. per 24 hours; serum electrolyte, urinary electrolyte, urea clearance values are listed in *Table 2.* Roentgeno-

Table 2.—*Laboratory data (case 2) obtained before and after treatment with benzydroflumethiazide*

Test	Treatment with benzydroflumethiazide			During Carter-Robbins test	Day of discharge from hospital
	Before	2 days after	5 days after		
Serum carbon dioxide, mEq./l.	22.3	25.3	23.7	—	28
Serum chloride, mEq./l.	1.2	99	103	—	102
Serum potassium, mEq./l.	4.8	5.0	3.5	—	3.3
Serum sodium, mEq./l.	143	140	145	—	138
Urinary potassium, mEq./l.	9.5	10.6	9.5	3.7	—
Urinary sodium, mEq./l.	4.5	30	10.0	10.5	—
Urinary chloride, mEq./l.	9.0	—	13.0	14	—
Urea clearance, ml./min.	98	—	109	—	—
Urine urea, mg./100 ml.	120	480	300	190	—

grams of chest, skull, and sella turcica were normal; electroencephalogram, paroxysmal slow dysrhythmia of subcortical origin, but improved in comparison to previous record; result of Carter-Robbins test shown in *Figure 3;* daily urinary output is graphed in *Figure 4.* There was an immediate response to 10 mg. daily of benzydroflumethiazide. Two weeks after discharge from the hospital the therapy became ineffective. Doses were increased to 15 mg. daily and produced some improvement, but the urinary output soon increased to 5000 ml. or more daily. Therapy now consisting of 5 mg. of benzydroflumethiazide orally daily, and 1 ml. of pitressin tannate intramuscularly every three or four days, adequately controls the polyuria.

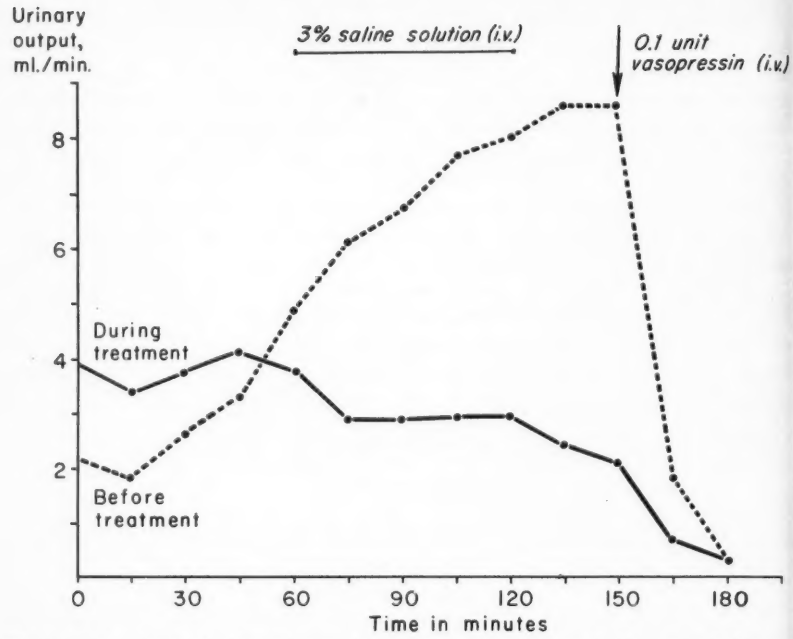

Fig 3. Case 2. Graph showing minute-urinary volumes in two Carter-Robbins tests before and during treatment with benzydroflumethiazide.

Carter-Robbins Test

The Carter-Robbins test is made after the patient has fasted for eight hours, and consists of hydrating the patient with 20 ml. of water per kilogram of body weight. If hydration is adequate, the urinary output rises to 5 ml. per minute. Then 3 per cent saline solution is injected intravenously, 0.25 ml. per kilogram of body weight per minute for 45 minutes. The urinary output is measured. Vasopressin,* 0.1 unit, is injected intravenously and the urinary volume is measured. The results of this test in our patients are shown in *Figures 2 and 3.*

In a normal person the hypertonic saline solution results in an output of vasopressin and a prompt decrease in urinary flow. In a person with diabetes insipidus there will be no decrease in urinary flow per minute following the injection of hypertonic saline solution. After the intravenous administration of vasopressin a notable decrease in the minute-volume of urine excludes the presence of renal diabetes insipidus. Because urinary output increased in our patients, after administration of 3 per cent saline solution, and a prompt decrease occurred after intravenous administration of vasopressin, the diagnosis of diabetes insipidus was proved.

**Pitressin, Parke, Davis & Company.*

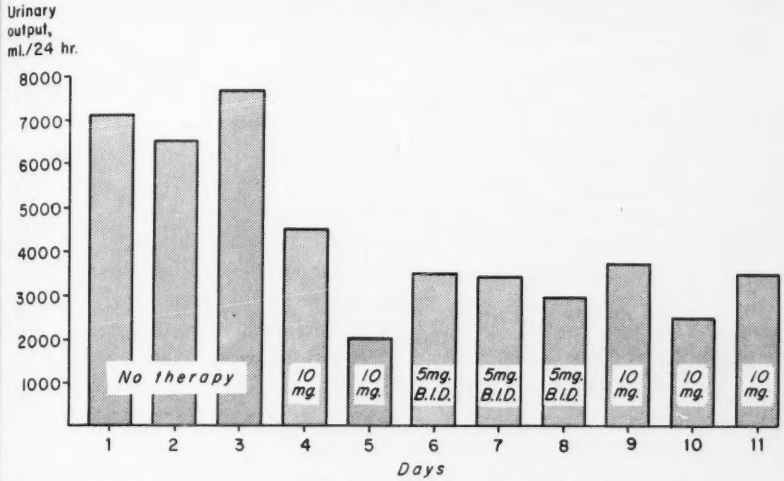

Fig. 4. Case 2. Graph showing the daily urinary volumes before and after treatment with benzydroflumethiazide in a four-year-old girl.

Comment

The responses of the 11 patients to benzydroflumethiazide therapy are similar to those reported by others[1-4] using chlorothiazide and hydrochlorothiazide. In our patients the daily urinary outputs decreased from an average of 7400 ml. to about 2000 ml., and became stabilized at about 2900 ml. The mechanism of decrease is not understood. In one patient *(case 2)* the Carter-Robbins test was performed while the patient was receiving 10 mg. of benzydroflumethiazide daily. The curve of the urinary output in *Figure 3* closely approximates the normal curve in *Figure 2*. The urinary potassium excretion, during the test, decreased to 3.7 mEq. per liter from previous values of 10.6 mEq. per liter obtained before the test. The concentrations of urinary sodium and chloride remained essentially the same as before the test.

The first-mentioned patient has been receiving 10 mg. of benzydroflumethiazide daily for six months. Although the urinary output (average, 3500 ml.) has not decreased to normal, it has been sufficiently controlled so that the patient remains comfortable. These patients have bladder capacities up to 500 ml., and seem well able to tolerate the large urinary output. On subsequent examinations the hemoglobin, leukocyte count, and serum electrolyte values have remained within normal limits. The urinary specific gravity has increased to 1.006.

The authors[1-4] who have demonstrated the effectiveness of chlorothiazide-like drugs in some patients with diabetes insipidus have recommended that the drug not be used routinely in clinical practice. We believe that the drug may be clin-

ically effective as long as it is used under close medical supervision.

Patients who receive posterior pituitary powder, as a "snuff," may acquire a local sensitivity in the nose with severe nasal stuffiness and even asthma. Occasionally the medication used intranasally will become ineffective and the patient must resort to intramuscular injections. Serious side-reactions to a sulfonylurea-like drug may occur when it is used as an antibiotic, an antihypertensive, an oral hypoglycemic agent, or as a diuretic. Under close supervision, however, it is used for these purposes without much hesitation.

Although diabetes insipidus rarely is harmful insofar as the patient's physical well-being is concerned, the symptoms certainly interfere with his living a normal life. Chlorothiazide-like drugs might well be useful in the clinical management of this problem. There has been no evidence of serious reactions to benzydroflumethiazide in our patients. The addition of the potassium chloride helps to prevent the development of severe hypokalemia, one of the major potential side-effects. The use of the drug has not changed the patients' sense of well-being nor has postural hypotension developed.

Many patients, particularly children, are extremely loathe to use either the nasal medication or the intramuscular preparation. Our patients were well satisfied with the form of medication as well as the clinical effects of benzydroflumethiazide, even though the urinary output did not decrease to normal.

Summary

A chlorothiazide-like drug, benzydroflumethiazide, was used in treating 11 patients who have diabetes insipidus. In seven, a definite decrease in the polyuria and polydipsia occurred; in four patients the drug was not effective.

It is our impression that the drug is useful in the clinical management of diabetes insipidus if the treatment of the patient can be closely supervised.

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BLOOD PROCUREMENT IN THE STATE OF OHIO

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IN the course of dealing with patients who are to have open-heart operations or other extensive operative procedures at our hospital, it has become apparent that almost every case presents individual problems from the standpoint of blood replacement. Such problems are largely those of geography, and are further complicated by the different approaches of communities to meeting their responsibilities to their people in providing blood procurement programs.

The simplest type of blood replacement is for the patient who resides in an area where an active community or Red Cross blood program exists. The most difficult type is for the patient who lives in a community without blood bank facilities, which is so far from our city that it is a hardship for his donors to come to our hospital bank. Fortunately, in most instances, the situation can be solved by having the blood collected from the donors at a hospital near the patient's home or at a hospital or blood center between the patient's home and Cleveland. Sometimes donors can be obtained in Cleveland through the activity of church, labor, or fraternal groups. Some areas provide cash payment for replacement of blood used by patients from their areas.

Because of the complexities of blood procurement, a map of Ohio was prepared to show the blood bank facilities that are available in various areas *(Fig. 1)*. Information for the preparation of this map was obtained from patients, their referring physicians, local pathologists, the office of the Cleveland Regional Blood Center of the American Red Cross,[1] the directory prepared by the Joint Blood Council,[2] the Guide Issue of Hospitals,[3,4] and by correspondence with several of the blood banks in this area.[5-7]

The greatest part of the state is covered by regional Red Cross centers or by active community blood banks. This represents 75 of the 88 counties in the state, and about 90 per cent of its population. Only 15 general hospitals, totaling about 2300 beds, operate in areas without community blood bank programs. The figures in each county represent numbers of hospital blood banks in each county. Only 11 of these hospitals have more than 100 beds. However, all 15 hospitals maintain active hospital blood banks, and in most cases draw all the blood they use from their own volunteer donors. Many of these banks are affiliated with the American Association of Blood Banks. Blood credit transfers between these banks and banks in other areas are possible through the Clearing House program of the American Association of Blood Banks. The policy of most of these banks is progressive, community-conscious, and sponsors giving help to local residents who have problems in replacing blood. Blood is willingly obtained from the donors

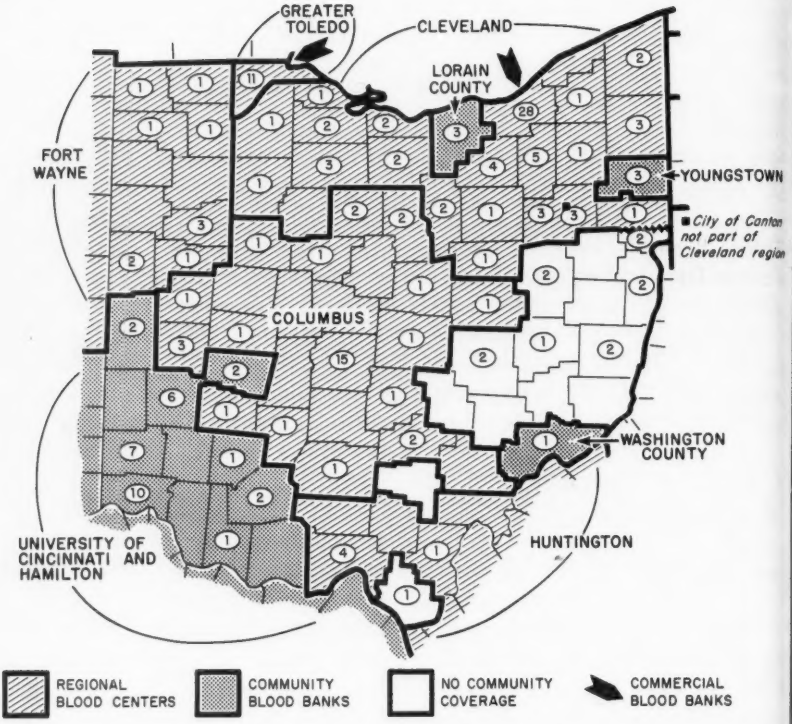

Fig. 1. Figures in ovals indicate number of blood banks listed for each county in the directory[2] or the listing of hospitals.[3] Stark County is shown separately for the city of Canton and the rest of the county. Columbiana County is shown divided, as only the northern parts of the county participate in the Red Cross program.

and is prepared for shipment. The city of Canton in Stark County with three hospitals and 738 hospital beds has no community program. Each of the hospitals has blood bank facilities. The Aultman Hospital has the largest bank, and this has been inspected and approved by the American Association of Blood Banks. East Liverpool in Columbiana County has no community coverage but is served by a highly community-conscious hospital blood bank. Many counties have multiple coverage and obtain blood from many sources. Indeed, few hospital blood banks in the state rely exclusively on any single source of blood.

There are five Red Cross Regional Blood Centers operating within the state. These are: the Cleveland Regional Blood Center, which serves most of the north-central and northeastern counties in the state; the Columbus Regional Blood Center, for much of the central area around the city of Columbus; the Greater

Toledo Regional Blood Center, for Lucas County; the Fort Wayne (Indiana) Regional Blood Center, for eight counties in northwestern Ohio in addition to a large area in Indiana; and the Huntington (West Virginia) Regional Blood Center, for five Ohio counties in addition to a large area in West Virginia and Kentucky.[5] Methods of exchange vary from center to center and sometimes within the individual regions.

The Cleveland area is the most active of the five centers, and processed 86,766 units of blood in 1959. It serves 173 cooperating hospitals.[2] The Greater Toledo Regional Center, the smallest in the state, was formed in 1958 to serve most of Lucas County.

The major community blood banks are those of the University of Cincinnati, which serves persons within an 80-mile radius of Cincinnati in Ohio, Indiana, and Kentucky.[6] Work in this area is supplemented by the Hamilton County Blood Bank, Inc.[7] No Red Cross or commercial blood banks operate in this area. It appears that there is some overlapping between this community program and the Columbus Red Cross group program in the counties on the periphery of the territory of each of these banks.

The Masonic Blood Bank in Dayton operates by paying for blood for their people; this has proved to be an extremely convenient repay plan. Several similar plans for fraternal and church groups are organized elsewhere in the state. The Lorain County and the Youngstown Hospital community blood banks do the excellent work of providing blood for people in their communities. The recently organized Washington County program in Marietta will fill a great need in that area of the state. Canton, although geographically within the Cleveland region, does not participate in the Red Cross program, but has had working agreements among the various hospitals and with the commercial blood bank in Cleveland, which have facilitated transfer of replacement credits from that area.

There are two commercial blood banks in the northern part of the state. Both of these banks play vital roles in supplying blood for the area. The Cleveland bank sells blood all over the northern part of the state, and the Toledo bank, which is a branch of a bank in Detroit, covers a similar territory. Commercial blood banks in Chicago, Detroit, Pittsburgh, and other cities are responsible for considerable quantities of blood used in the state either by direct purchases or by accepting blood donations for our patients and then crediting such donations to our account. Patients in western Pennsylvania can make replacements through the blood bank at St. Vincent's Hospital in Erie, Pennsylvania, which has a license from the National Institutes of Health and can ship blood out of Pennsylvania. Meadville (Crawford County), Pennsylvania, participates in the Buffalo Regional Red Cross Blood Center program, while most of the rest of this area is covered by the Central Blood Bank of Pittsburgh, the Johnstown Regional Red Cross Blood Center, or the Beaver County Regional Red Cross Blood Center, all in Pennsyl-

vania. The West Virginia counties along the Ohio River, north and east of Pleasants County, have no community coverage.

Discussion

The problem of supplying blood to patients in Ohio has been solved in the typical American fashion of each community's deciding what is best for itself and then going ahead and doing something about it. No significant difficulties arise from the various locality differences; and, with the recent understanding between the American Red Cross and the American Association of Blood Banks, the few difficulties that are present will be further diminished. The areas of the state that have no community coverage are usually sparsely populated areas in which medical services are not up to urban levels. For treatment of serious illnesses and for major operations, people from such areas are usually transferred to nearby urban centers where more adequate medical care, including blood supply, is available.

No one means of donor procurement would supply the blood needed in Ohio. Blood is obtained for the state as a whole through three principal sources: volunteer donors (Red Cross, community, or hospital banks), repayment donors, and professional donors. Volunteer donors supply about 40 per cent of the blood for our own hospital; these donors are recruited and the blood is drawn by the American National Red Cross. Repayment donors supply about 20 per cent of the blood for our hospital, and the remaining 40 per cent comes from professional donors recruited from our own donor lists or through one of the commercial blood banks in the area. Each type of donor procurement has advantages and disadvantages. It is probable that in our hospital we would be unable to get along with any one type of procurement, and that for most efficient blood bank administration there must be judicious use of all three means of procuring blood.

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INSTRUCTIONS TO THE COLOSTOMY PATIENT

Management of the Colostomy

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EVERY colostomy patient is instructed in the care of the stoma while in the hospital. The following pamphlet is given to the colostomy patient by the enterostomal therapist who personally instructs each patient.

Instructions to the Patient

The objective of this pamphlet is to teach you to empty the colon completely by an enema. In most adults, the colon when emptied completely does not fill for two days. Therefore, if the emptying is complete, you could expect to have no movement except during enemas that are given every second day. In some patients, the colon fills rapidly, and it is therefore necessary to irrigate the colon every day. We shall help you to decide how often you must irrigate the colon.

Some patients have an "irritable" colon. An irritable colon has cramps and excessive gas formation, and the bowel movements are not always predictable; a movement may occur at any time, particularly after meals, or there may be constipation and no movements. This unpredictable pattern of movements may be a lifelong habit. For such a person, irrigation may not be the best way to manage the colostomy. Perhaps you belong to this group of patients, and you should not irrigate your colostomy. Perhaps you should allow the bowel to move spontaneously; this may occur at fairly regular intervals. Whether or not you are going to control your bowel movements by irrigation will depend on the type of colon you have. However, while you are in the hospital, we are going to acquaint you with the technique of irrigation. You will be using the Greer enema compact *(Fig. 1)*.

Irrigating the Colostomy

1. Put on the plastic irrigating sleeve, centering the stoma in the middle of the metal ring, and fasten the belt.

2. Fill the white rubber enema bag *(Fig. 1A)* with one quart of warm water and hang it about five feet from the floor on a hook. (If you are not at home, a hook can be fashioned from a wire coat hanger.) Remove all air from the tubing by releasing the shutoff valve *(Fig. 1B)* and allowing water to run from the bag through the hose and out the tip of the catheter. Put Vaseline on the end of the catheter.

3. Insert your finger into the colostomy and determine in what direction you will be inserting the catheter. Cautiously insert the catheter *(Fig. 1C)* into the colostomy for two or three inches, allowing the water to run all the while to clean out the lower

Acknowledgment is made to Mrs. Norma Gill, Enterostomal Therapist, the Cleveland Clinic Hospital, who assists the patient to learn how to take care of his colostomy.

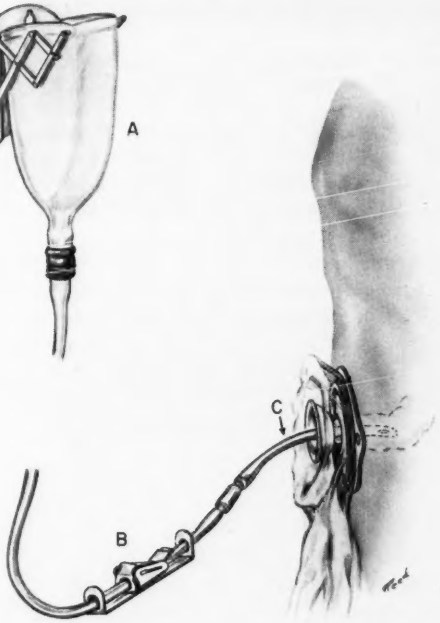

Fig. 1. Greer irrigating apparatus: A, Water container. B, Shutoff valve. C, Irrigating catheter.

five or six inches of colon. (Never force the catheter into the colostomy but push it gently, feeling your way along with the water running briskly.)

4. Refill the white enema bag with a quart of water, or more if you wish. After filling the tubing with water, insert the irrigating catheter again. Push the shield or dam tightly against the colostomy so that the water will not leak around the tubing. Allow the water from the bag to run slowly. If a cramp develops, stop the flow of water until the cramp passes and then allow more water to flow. Most people can take a little less than a quart of water but some can take more. When the enema is completed, remove the catheter, and fasten the top of the irrigating sleeve with clips. Note that it is important to get as much water as possible into the colon at the time of irrigation, because this will stimulate the colon to contract and to empty. Too little water gives too little returns.

Most patients wait about 15 minutes with the drainage sleeve in the toilet. Some of the water will have returned by this time. Then rinse the drainage sleeve with water from a pitcher, or fill the bag with water and let it run down through the sleeve. Fold the bottom of the sleeve up against the top of the apparatus and fasten with clips so that you can leave the bathroom.

During the 45 minutes following this first irrigation, most of the water will return.

5. About 45 minutes after you have completed the irrigation, apply the colostomy

cap that is in your set. Put some facial tissues inside of the cap and place it over the colostomy to catch any extra returns of mucus or water. You should stop using this cap as soon as possible, because it encourages the colostomy to protrude. A square or two of gauze held in place directly over the colostomy by an elastic waistband is ideal.

Discussion

If you allow the water to run too rapidly into your colon, or if you use too much water, or if the water is too cold, you may feel faint and become sweaty or dizzy. Sometimes vomiting results.

Occasionally, after the water has been run into the colon it will not come out until three or four hours later, and then only in small amounts repeatedly. This means you have an irritable colon. Remember the colon may only be irritable when *you* are irritable or apprehensive or worried. It may act normally at other times. We will give you medications to alleviate this condition should it become necessary.

If all of the water put into the colon does not return, do not be alarmed, since this water is simply absorbed and in the ensuing hours the bladder will fill and empty more frequently.

You must be careful never to force the catheter up into the colon against any obstacle. You could perforate the colon and cause peritonitis. The colon has no nerves and, consequently, perforation does not always produce immediate pain. However, should severe pain develop after a difficult catheter passage, call one of us or your own doctor on the telephone. Fortunately, perforations are rare. To prevent this catastrophe you are given a French-24 Foley catheter to use for irrigation. Note that the end of it is quite soft.

Remember that the entire irrigation procedure is simply a *thorough cleansing enema* and some time is required to empty the colon. Do not forget that it takes water to get water. The colon must be completely empty or you will surely have additional bowel movements following irrigations. Do not be discouraged if you do not promptly learn how to irrigate the colon, as it takes several weeks before one can be considered expert.

Variations in Irrigating Technique

The method of irrigation described above is presented only as a guide; your irrigating technique should be individualized. For example, you may want to start with a pint of water and repeat the insertion of a pint after each return. Or, perhaps you you would like to use more than a quart of water for the first irrigation. Or possibly you would like to put a quart — or pints — in repeatedly following each return. These are some of the variations in techniques to use.

Occasionally salt or soda may be added to the irrigating water. Some patients add a tablespoonful of salt to each quart of irrigating water. If you wish, we will supply you with an enema powder known as *Lavema* made by the Winthrop Company; Lavema can be purchased at your local drug stores. One-half the contents of an envelope in one quart of warm water is the approved mixture. Lavema stimulates the intestine so that the return after the enema is more prompt. It generally is harmless, but if nausea

and vomiting or intestinal cramps occur, simply use less powder.

Care of Irrigating Apparatus

The irrigating equipment that we use most frequently is the *Greer Colostomy Compact.* Instructions for its care come with the apparatus. Should any part become damaged (cracked or leaky), be sure to exchange it. The Cleveland Clinic Pharmacy stocks the apparatus, or the Greer Company will supply you with the address of your nearest dealer. You may write to:

Greer Manufacturing Company
3805 Broadway
Oakland 11, California

Diet

You have been supplied with a diet sheet that should be followed for about six weeks after your discharge from the hospital. The diet simply omits foods that cause gas (peas, beans, cabbage, fish) or frequent bowel movements (fruit, fruit juice, and vegetables such as green spinach and tomatoes). There may be some other foods that you personally should avoid — you will already be aware of these foods.

Six weeks after your discharge from the hospital, you should return to what you consider a normal diet. You will find that some foods still cause diarrhea or gas and you may have to omit them permanently.

Bathing

You may take a bath or a shower at any time. The colostomy can be submerged. Do not be alarmed if there is a little bleeding from around the edges from time to time. This is natural. Do not try to sterilize the skin around the colostomy with iodine, alcohol, or antiseptic solutions. Treat it as any other part of the body with soap and water. Do not use sterile dressings.

CLEVELAND CLINIC COLOSTOMY DIET

Foods Included:	Foods Excluded:
	Fruits
	Fruits in any form, cooked or raw. All fruit juices except nectars.
Cereals	
Cream of Wheat, farina, Wheatena, barley, oatmeal, Cornflakes, Puffed Rice, Puffed Wheat, Rice Krispies, Shredded Wheat, Muffets.	Those containing bran such as All Bran, 40% Bran Flakes.
Breads	
White, refined whole wheat, graham, or rye; simple wafers or crackers; Arrowroot crackers; Melba Toast, Zwieback, Holland Rusk; rolls, muffins, baking powder biscuits, waffles, pancakes.	Cracked-wheat bread; bread, muffins or rolls made with bran; bread or rolls with nuts, dried fruits such as raisins. Muffins made with fruit such as blueberry muffins.
Eggs	
Soft boiled or hard boiled, poached, scrambled, omelet, fried, creamed, or as soufflé.	
Soups	
Cream soups made of rice, potato, or allowed vegetables. Clear broth or broth with noodles or rice. Strained broth from soups made with vegetables such as corn or mushrooms.	Whole vegetable soups made with other than allowed vegetables.
Meats	
Beef, lamb, veal, pork, ham, liver, sweetbreads, bacon, domestic rabbit, loose sausage, luncheon meats, chicken, squab, turkey, duck, goose, oysters. Fresh, smoked or canned fish. Meats may be fried, boiled, broiled, or roasted.	
Potatoes, etc.	
White potatoes — baked, mashed, boiled, creamed, escalloped, or fried. Sweet potatoes, spaghetti, noodles, macaroni, rice, hominy.	Potato skins.

CLEVELAND CLINIC COLOSTOMY DIET—*Continued*

Foods Included:	Foods Excluded:
Vegetables (cooked) Asparagus tips, celery hearts, cauliflower tips, squash (no seeds or skins), rutabagas, turnips, puréed beets and carrots. Crisp tender lettuce is the only raw vegetable permitted. Vegetable juices, such as V8, tomato, and carrot.	Salads except tender lettuce. Green vegetables such as broccoli, Brussels sprouts, peas, spinach, tomatoes, corn, cabbage, string beans, wax beans, green lima beans, mushrooms, dried beans. (All of these vegetables may be used in puréed form, but produce gas.)
Desserts Custards, puddings, plain cakes and cookies, ice cream, gelatin desserts; pastries such as cream puffs; pies such as custard or chocolate cream.	Any dessert containing fruits, nuts, or coconut, such as fruit cake, fruit pies, mincemeat pie, raisin pie, sherbets, fruit whips, coconut cookies.
Beverages Coffee, tea, Sanka, Kaffee Hag, Postum, milk, milk beverages such as milkshakes, eggnogs, and malted milks. Carbonated beverages. Wines and hard liquors also are permitted.	
Miscellaneous Cheese may be used as desired. Any fats as butter, margarine, oils, salad dressings, cooking fats. Smooth peanut butter. Potato chips, pretzels. All seasonings and condiments such as catsup and mustard. Jellies, honey, syrups, molasses, and candies. Gravies and white sauce.	Popcorn. Relishes made of raw vegetables such as piccalilli or pepper hash. Jams and marmalades. Pickles, olives, and nuts. Any other foods which you may find will cause diarrhea.

NOTE: The colostomy diet is one of personal management. This diet is a guide in that it shows you which foods are most likely to be tolerated and which ones are not.

SAMPLE MENU

Breakfast:

CEREAL
. . . Cream of Wheat
EGG
. . . Poached egg with bacon
BREAD
. . . Toast with butter and jelly
BEVERAGE
. . . Coffee, cream and sugar

Luncheon:

MEAT OR SUBSTITUTE
. . . Cheese soufflé
POTATO
. . . Baked potato
VEGETABLE
. . . Buttered asparagus tips
BREAD
. . . Whole-wheat bread and butter
DESSERT
. . . Ice cream
BEVERAGE
. . . Milk, coffee, or tea, as desired

Dinner:

SOUP
. . . Chicken rice soup
MEAT
. . . Roast beef with gravy
POTATO
. . . Mashed potatoes
VEGETABLE
. . . Buttered puréed beets
DESSERT
. . . Plain cake
BEVERAGE
. . . As desired

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